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VOLUME XXXI NUMBER 4

DISEASES

of the

CHEST

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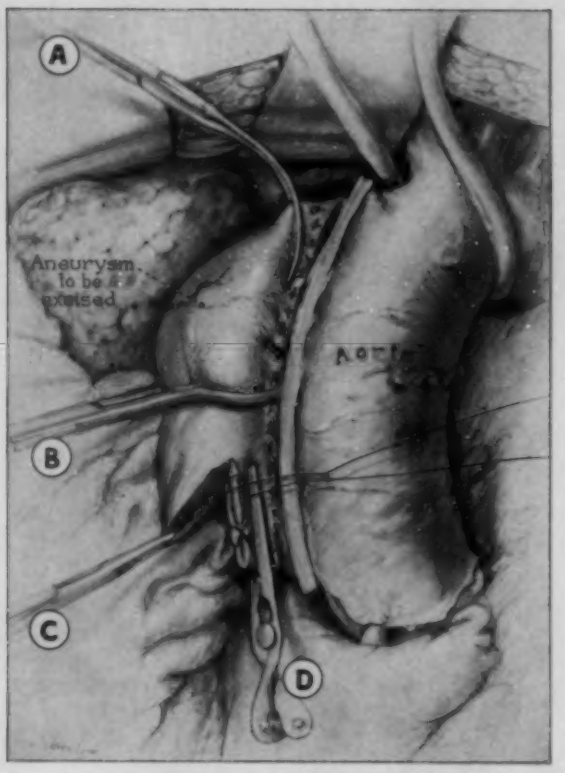

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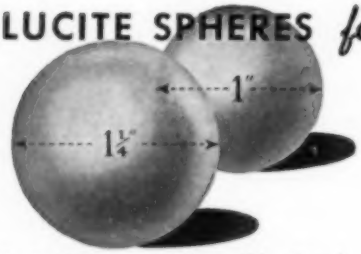

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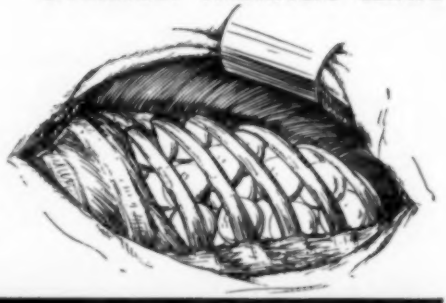

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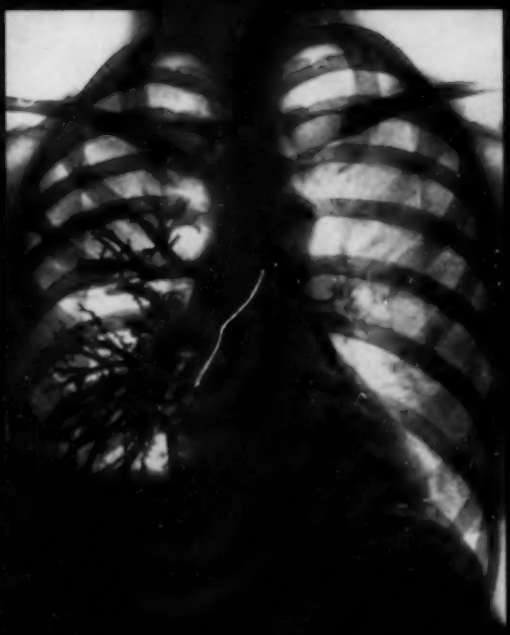

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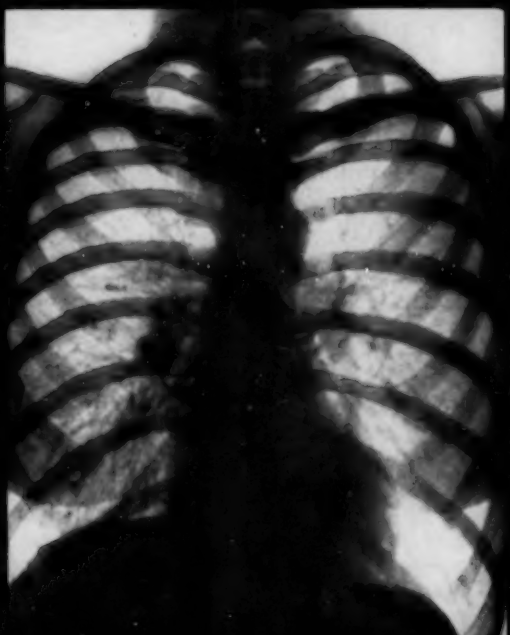

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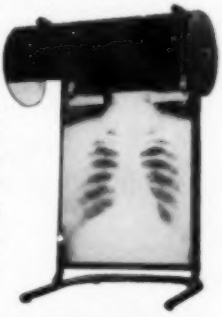

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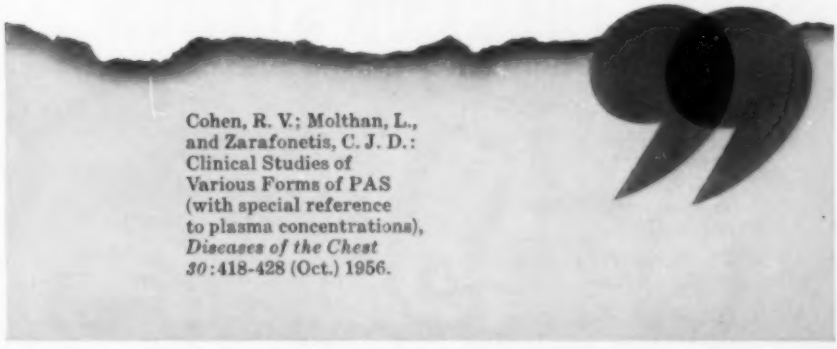

Cohen, R. V.; Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations), *Diseases of the Chest* *30*:418-428 (Oct.) 1956.

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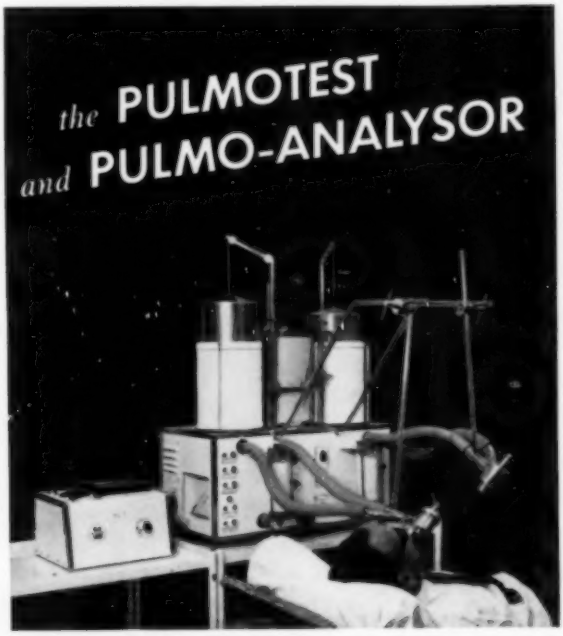

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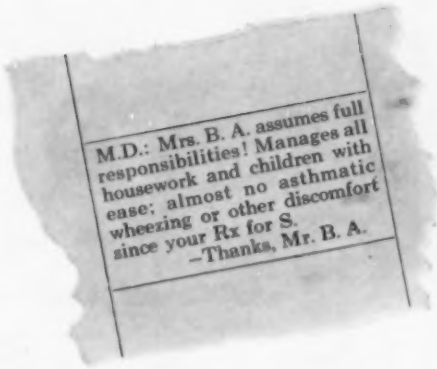
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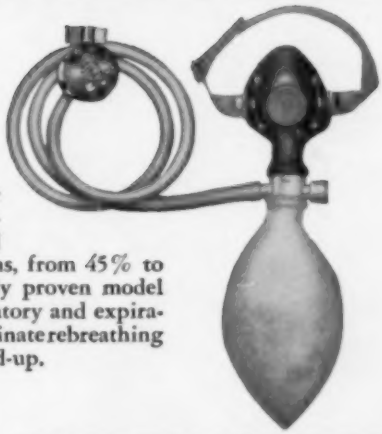

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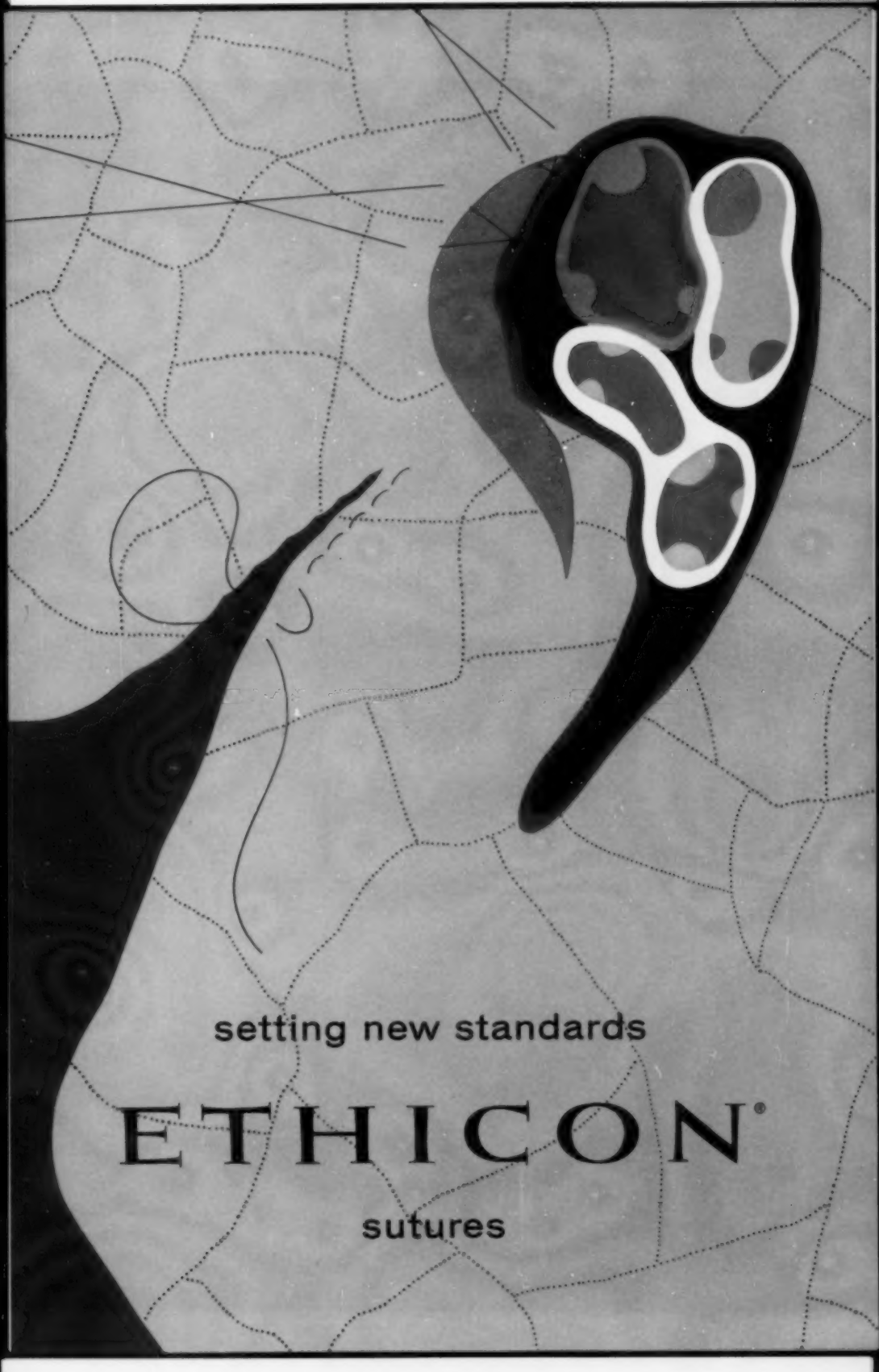
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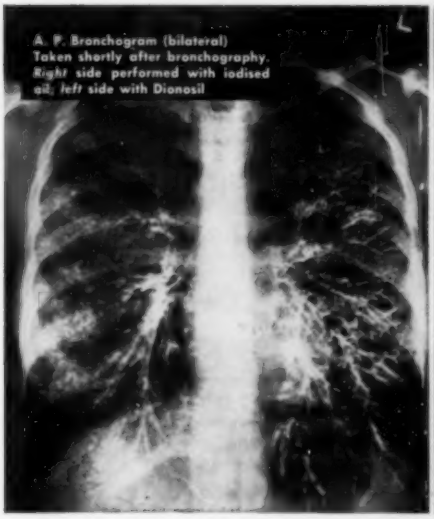

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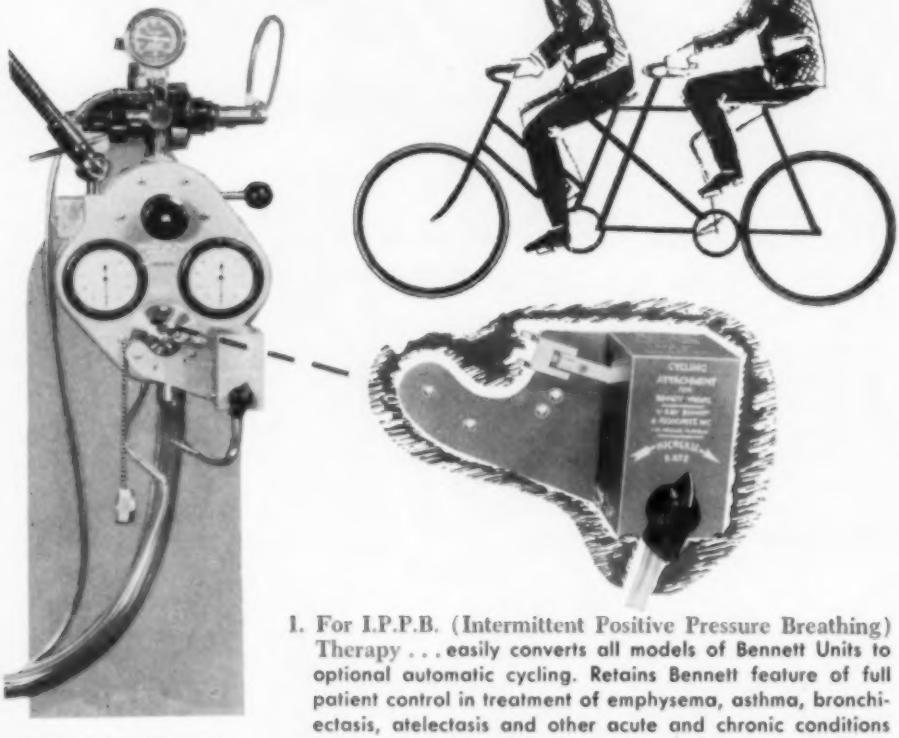

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DISEASES of the CHEST

VOLUME XXXI APRIL, 1957 NUMBER 4

Cardiovascular and Pulmonary Physiology*, **

BURGESS L. GORDON, M.D., F.C.C.P.

Philadelphia, Pennsylvania

The era of the dread infections has passed and it may well be said our people today are more healthy, more energetic than any previous generation in the history of the world. We are grateful to preventive medicine and chemotherapy for having initiated this great evolution and given to us the tools with which we may deal in hand-to-hand combat with infectious diseases wherever and whenever they appear. Indeed the empirical methods of therapy and the uncertain concepts of etiology are being replaced and future students of medicine may never know, except historically, about disease that once was ill-defined, rampant and uncontrolled.

No one is more conscious of this evolution than the internist with a special interest in the chest, for he is the one who dealt with tuberculosis, empyema, and rheumatic fever when these conditions were in the ascendancy. But in the same vein it should be mentioned that modern diagnosis and therapy have not resolved our health problems. Why? Because there has appeared simultaneously with increasing longevity an avalanche of degenerative pulmonary and cardiac conditions, not altogether amendable to specific therapy.

Of great interest is the increased number of pulmonary and cardiac conditions now classified as physiopathologic disturbances, in which the pathology is represented more as a healed process of antecedent infection rather than new disease; as for example, retracted mediastinum, displaced heart, thickened pleura, atelectasis, and emphysema with associated fibrosis. Indeed chest medicine is now vigorously challenged to "face-up" to the problems of disturbed physiology that our people may reach out for greater longevity.

An interesting aspect of the problems of disturbed cardiopulmonary physiology is that the symptoms are reflected chiefly in terms of discomfort in living, gradually increasing disability, and a peculiar susceptibility to bouts of intercurrent infection with lingering convalescence. In these cases structural alterations of the lungs, heart and pleura may not be present in any significant degree; indeed they often are disproportionate to the symptoms. It is in this connection that the term "disturbed function" has superseded disease *per se* as the cause of illness. With reference to the lungs, the chief difficulties relate to fibrosis, diffuse or generalized, with the concomitant

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loss of elasticity, over-distention, bronchoalveolar infections, bronchospasm, relative inefficiency of the pulmonary circulation, and the inevitable physiological disturbances involved in gas exchange; i.e., the transport of oxygen through the alveolar membrane to the general circulation, and the discharge of carbon dioxide along the reverse pathway. And with the heart there is the havoc of cor pulmonale, valvular defects, and coronary disease.

The clinical features of pulmonary and pleural disease at first may be so masked as to be entirely overlooked. The first clues may be faulty posture, a gradual increase in the circumference of the chest, and the excessive use of thoracic breathing, with a corresponding disuse of the diaphragm, paroxysmal cough, bouts of expectoration, dyspnea on exertion, and weakness. The ultimate trends are disability in the true sense of the word with physiologic failure, resulting in the retention of residual air, correspondingly low oxygenation, and resistance in the pulmonary circulation.

The physiologic aspects of the lungs are exemplified in the considerations of emphysema. It is said of this condition that the residual air percentage of total lung volume increases principally at the expense of the complemental air percentage of total lung volume; and the percentage of portions of the lungs occupied by supplemental or reserve air and tidal air remain nearly constant, regardless of the degree of emphysema. The breathing reserve may be noticeably reduced, since the depth of inspiration is increased only slightly above that of the resting state. There is also faulty distribution of air in the lungs, resulting from the unequal aeration and perfusion caused by the fibrotic and obstructive changes in the lungs. Poor distribution of air lowers the arterial pressure of oxygen and percentage of oxygen saturation, owing to the drop in mean pressure of oxygen between the alveolus and the arterial blood. In some cases, the increased mean gradient of pressure for oxygen between the alveoli and arterial blood approaches 50 mm. of mercury (normal, 5 mm. of mercury), and the average resting arterial oxygen saturation is moderately reduced but poorly correlated with impairment of pulmonary function. Interestingly, the arterial oxygen values obtained during mild exercise may reveal significant differences with respect to disability and the degree of emphysema, as illustrated when the arterial oxygen value is compared with the resting level.

The heart may be disturbed as a result of primary disease, as in valvular defects, coronary insufficiency, and pericardial involvement; or it may be affected by disturbed function as to rate, rhythm and force of contraction. These alterations display their own peculiar patterns of disturbed function, problems that may be classified broadly as cardiac insufficiency. The aspect to be emphasized is that the behavior of the heart may be greatly disturbed by diseased lungs, and vice versa the lungs may be influenced by the abnormal heart. Increasingly we have come to think of the heart and lungs as closely associated in the complex ramifications of physiologic function.

It is considered logical in the light of our present knowledge of cardiopulmonary physiology, modern thoracic surgery and chemotherapy to

assume a dynamic approach in dealing with chronic pulmonary diseases and defects of the heart. With reference to the lungs, the success of physiologic therapy emphasizes the importance of this consideration. As illustrated repeatedly, preceding the advent of chemotherapy drainage with long periods of rest was the accepted procedure in treatment of pleural suppuration. While the immediate response was satisfactory, the ultimate course often was characterized by thickened pleura and contraction of the lung; pulmonary disability was inevitable. Gradually it became apparent that adequate expansion of the lung was as vital for satisfactory convalescence as was the control of the pleural infection. And various surgical procedures, including decortication, with or without thoracoplasty have become increasingly employed.

The value of physiologic management of the impaired lung is emphasized by results attained through the use of breathing exercises, intermittent positive pressure breathing treatments, abdominal compression and thoracic surgery.[1, 2, 3, 4, 5, 6] The goal is to restore pulmonary elasticity, facilitate bronchial drainage, and to improve the excursions of the lungs and diaphragm. With these accomplishments the transport of oxygen and carbon dioxide through the aveolar membrane may be definitely improved. Progress is manifested at first by checking the downhill course of physiologic disability, followed by reclamation of impaired alveoli and bronchioles. This improvement varies individually, beginning with control of the pathologic processes to the actual stage of rehabilitation, whereby there is a gain of one-eighth or more of function capacity and/or symptomatic relief. In certain instances there is graphic display of improvement that parallels the clinical course; as for example, a decrease of rales, increase of thoracic excursions, greater movement of the diaphragm, a rise in the vital capacity and reduction of residual air, all minimal but nevertheless definite. The features may remind one of the aging athlete who has become "soft," with loss of muscular coordination. A devotee of the rocking chair, his longest walk is from home across the driveway to his parked automobile. The first principle for reconditioning is to begin a graduated course of calisthenic exercises and walking on level ground—not overdoing at any time. New reserves and better "wind" with greater agility follow.

Physiologic studies should precede the use of dynamic treatment of degenerative pulmonary disease and cardiac surgery. But they should complement rather than supersede the stethoscope and other accepted methods of examination and testing. The stethoscope especially remains invaluable for interpreting the effects of disturbed physiology.

The chest physician stands in the midst of an interesting and most challenging array of pulmonary and cardiac diseases, the solution of which ultimately may well be a mighty contribution to better health especially of older people.

SUMMARY

The specific pulmonary infections, notably pneumonia and tuberculosis, have been largely controlled by preventive medicine and chemotherapy. But there has developed in the wake of these medical accomplishments, increas-

ingly, a group of pulmonary diseases such as emphysema, fibrosis, bronchiectasis and chronic pleurisy. These conditions are especially noted in older people, reflecting as they do the occurrence of antecedent disease with aggravation and the influences of degenerative processes of aging tissues. Disturbed cardiopulmonary physiology results in physical disability and calls for timely physiologic testing and dynamic treatment.

RESUMEN

Las infecciones pulmonares específicas principalmente la tuberculosis y la neumonía se han dominado en general por medio de la medicina preventiva y de la quimioterapia. Pero al mismo tiempo que esto se ha logrado, un grupo de otras enfermedades pulmonares como el enfisema, fibrosis, bronquiectasias y pleuresías crónicas han aparecido de modo creciente.

Estos padecimientos son notables especialmente entre la gente de edad avanzada siendo en ellas un reflejo de enfermedades antecedentes y la influencia de los procesos degenerativos en los tejidos envejeciendo. La fisiología cardiopulmonar perturbada produce incapacidad física y requiere oportunas pruebas fisiológicas y tratamiento dinámico.

ZUSAMMENFASSUNG

Die für die Lungen spezifischen Infektionen, nämlich die Pneumonie und die Tuberkulose, sind in grossem Umfang in unserer Hand dank der praeventiven Medizin und der Chemo-Therapie. Aber im Kielwasser dieser ärztlichen Fortschritte hat sich eine in ihrer Zahl sunehmende Gruppe von Lungenkrankheiten entwickelt, wie z.B. das Empsysem, die Fibrose, die Bronchiektasie und die chronische Pleuritis. Diese Zustände werden besonders bei älteren Leuten beobachtet und sie spiegeln das Vorkommen vorausgegangener Krankheiten mit Verschlechterung sowie die Einflüsse degenerative Prozesse der alternden Gewebe wider. Störungen im normalen cardio-pulmonalen Geschehen haben physisches Unvermögen zur Folge, sodass sich die Forderung nach einer rechtzeitigen Funktionsprüfung und dynamischen Behandlung erhebt.

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The Management of Tracheal Stenosis With a Case Report

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Post traumatic stenosis of the intrathoracic trachea is a relatively uncommon condition, but when it occurs it presents a grave challenge to the thoracic surgeon. A similar condition in the major bronchi is not only more common but equally applicable as far as treatment is concerned, and it is from this that most of our knowledge on the subject has been obtained.

Successful repairs of ruptured or lacerated tracheas[1, 2] and of ruptured main bronchi[3] have been reported without the sequela of stricture, but when there is actual tissue loss or the tear is unrecognized or not repaired, stricture formation is almost certain.

Once stricture of the trachea is present, temporary relief of the respiratory distress can usually be obtained by dilatation and, if necessary, intubation, but permanent cure is most unlikely to be achieved by anything short of definitive resectional surgery.

A fairly extensive literature on the subject of resection of stenosed segments of the air passages has accumulated in recent years; its applicability to stenosis from carcinoma and tuberculosis, as well as post traumatic causes, is well recognized.

Much experimental work on the replacement of these resected segments by various types of grafts and prostheses has been done, mostly in dogs, and critical appraisal of the various methods and techniques used suggests that we are still a long way from solving the problem completely.

Recent work on this subject makes a review of the literature superfluous. This has been adequately covered by Paulson,[4] Abbot et al,[5] Thompson et al[1] and many others. However, consideration of the many available papers shows that certain basic facts emerge on which the principles of tracheal surgery must be based.

Annular removal of a segment of trachea or bronchus and subsequent repair of the defect by an autogenous graft of some kind inevitably results in eventual stenosis of the grafted area if no prosthesis is used to prevent contraction.[6, 7]

The successful use of a prosthesis alone to bridge tracheal defects has been reported in dogs,[8, 9] but, for reasons to be discussed later, this is not the most suitable method. It would appear that the best results are obtained by some technique which utilizes autogenous tissue grafts such as fascia

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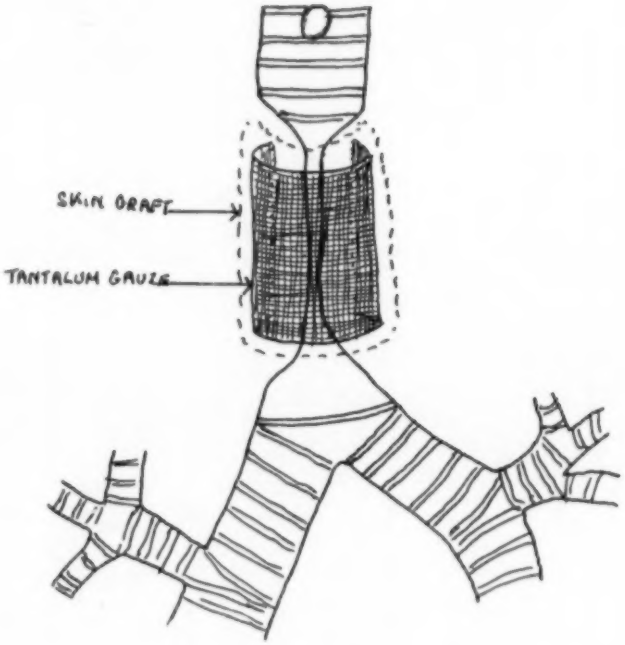

FIGURE 1

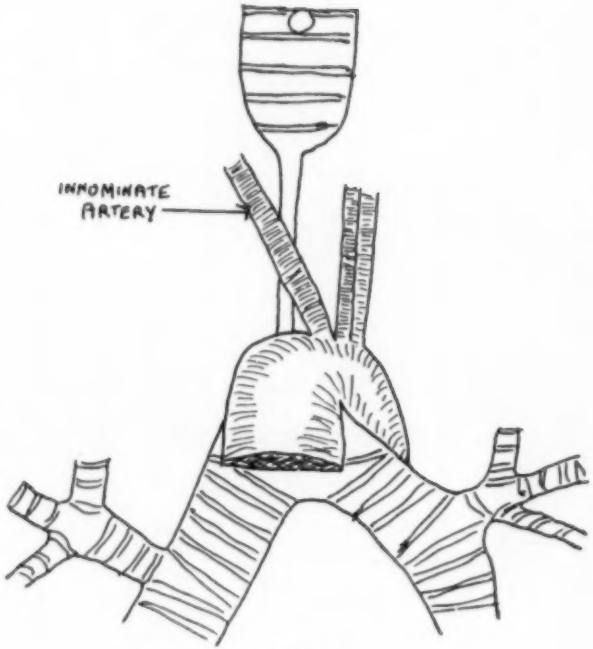

FIGURE 2

Figure 1: The extent of the stricture showing superimposed graft and tantalum gauze.—*Figure 2:* Superimposed great vessels to show the relationship of the innominate artery to the stricture.

lata,[10] pleura,[11] skin[4, 12, 13, 14] or other structure and at the same time provides for maintenance of their rigidity by a prosthesis. Of these, full thickness skin is probably one of the most satisfactory materials because of its toughness, pliability and availability.[15] Tubular types of prostheses made of metal, glass or plastic, either alone or in conjunction with autogenous grafts, have been used occasionally to bridge large defects, but the frequent failure of these forms of support lies in the fact that they must perforce remain as foreign bodies within the lumen of the trachea—a constant source of irritation and potential sepsis. Furthermore, their removal at a later date, even though the tissues are otherwise satisfactory, would appear to lead to inevitable stenosis.

The best results have been obtained when the rigidity was maintained by some latticed or open work prosthesis which allows granulation tissue extrusion through the gaps and subsequent epithelialization within the lumen, i.e., stainless steel wire,[17, 18] tantalum gauze,[19] etc. which eventually becomes incorporated within the new wall as an inert strut. The probable reason for the comparative success of this type of prosthesis is that a relatively inert material, like stainless steel, tantalum or plastic, once embedded completely in fibrous tissue, is unlikely to give trouble, but when part of it projects into a space, namely the bronchus, which is potentially infected, trouble in the form of chronic suppuration will inevitably ensue.

Certain other technical points in the repair seem to be important—the airtightness and watertightness of the graft during the whole postoperative course so that air will not leak out or fluid leak in,[20] and, also, the avoidance of clamps on the bronchus or silk in the suturing, which experimental work on animals has shown conclusively to encourage fibrosis and stenosis.[21, 22]

The case which most nearly approximates ours is that described by Edgerton and Zovickian.[13] Their defect was slightly larger than ours, namely 7 cm., and their hemorrhage, from the right common carotid at the site of the ligated right vertebral artery stump, occurred on the twelfth postoperative day.

Case Report

A 20 year old married white woman was involved in an automobile accident on August 11, 1955. The initial treatment was in another part of the country, and we are indebted to Dr. Lyle H. Prenzler of Bloomington, Illinois and Dr. Joe H. Henshaw of Sweetwater, Tennessee for the details of the management of the case prior to her coming under our cognizance.

She sustained a fracture of the mandible, a fracture of an ankle, severe crushing of the whole thorax (but no demonstrable bony injury), left tension hemopneumothorax and right hemopneumothorax. There was marked mediastinal widening radiologically and subcutaneous surgical emphysema in the tissues of the neck. In view of the fractured jaw and the appalling condition of the chest, tracheostomy was wisely performed, and she appeared to progress satisfactorily.

On the 14th day after the accident, the tracheostomy tube was removed and apparently breathing was not obstructed. By September 6, i.e., 26 days after the accident, the tracheostomy stoma had closed and she had marked nocturnal dyspnea. The stoma was reopened and an adult size Foregger tube was inserted through it down the bronchus with immediate relief. A short time later, she was moved to this area and admitted October 31, 1955, under our care as an emergency with extreme dyspnea.

When first seen, she was unconscious and the tracheostomy stoma was partly open, the Foregger tube having been removed a few days before. An immediate bronchoscopy through the tracheostomy stoma was performed in bed on this almost dead patient, and a complete obstruction of the trachea, about 3 cms. below the stoma, was observed. The

bronchoscopic suction tip was forced through the mass of granulation tissue and oxygen given through it. The bronchoscope was then withdrawn and a number 22 Foregger endotracheal tube was forced through the stricture; she again became conscious. Breathing through this small tube was just sufficient to keep her alive, but about nine hours later, in the early hours of the morning, she again obstructed and required further emergency bronchoscopy. This time it was possible to insert a slightly larger Foregger tube; during the next few days successively larger ones were introduced and she could breathe without obstruction.

Up to this stage the carina and main bronchi had not been visualized, but on November 5, 1955, bronchoscopy was performed with this idea in mind. The trachea at the site of the stricture admitted the 6 mm. x 40 cm. bronchoscope fairly easily and, as the carina and main bronchi were seen to be normal, it was decided to remove the Foregger tube and see how she managed. She was discharged home at her own request and arrangements were made to readmit her in five days for further bronchoscopy and assessment of the condition.

When she was readmitted on November 11, 1955, she was again having trouble getting her breath. Bronchoscopy revealed an almost similar condition as had been visualized at the second examination; again a number 22 catheter was the largest that could be inserted through the stricture. On this occasion, the granulation tissue was painted with 15 per cent silver nitrate. During the next few days it was possible to insert larger and larger tubes through the stricture until, by November 18, 1955, a number 32 Foregger tube was in place and she had no dyspnea.

On November 21, 1955, bronchoscopy was again performed through the tracheostomy opening. The distance from the lower edge of the tracheostomy to the carina was 7½ cms.; for 7 cms. of this, the whole lumen was filled with granulation tissue. The area was touched with silver nitrate and the Foregger tube replaced down to the carina. Posteroanterior and lateral laminagrams gave excellent pictorial confirmation of the extent of stricturing.

For the next three weeks she was comfortable, had an adequate air exchange through the Foregger tube, and was as ambulant as her injured ankle allowed. During the last 10 days of this period, she was given chloromycetin and erythromycin (which sensitivity studies of her bronchial secretions had shown to be most effective) in an endeavor to reduce the sepsis in the granulation tissue.

Bronchoscopy was again performed on December 13, 1955, i.e., four months after the original accident, and a most marked change was evident. The 5 mm. x 30 cm. bronchoscope passed easily through the previously strictured area, which was now smooth and healed except for two small areas of residual granulation tissue. As there appeared to be no gross stricture, it was decided to remove the Foregger tube and see how she progressed.

With the tube removed and the tracheostomy covered over, she breathed easily and well and, for the first time, we began to feel optimistic. However, this was short lived. Three days later she again had severe dyspnea; bronchoscopy revealed stenosis almost as bad as when she was first seen. It was finally decided that only definitive surgery could offer any hope of cure, and that same evening operation was performed. *Operation:* Dr. Waterman; *General Anesthesia:* Dr. G. Finer.

With the patient in the supine position, induction of the anesthetic was begun with pentothal; within a few minutes she became extremely cyanised and, in order to obtain an adequate airway, it was necessary to reopen the tracheostomy and pass a bronchoscope forcibly through the stricture. This was replaced by an endotracheal tube, the anesthetic continued, and a vertical incision made which encircled the tracheostomy opening and continued down over the suprasternal notch to about the fifth interspace. The internal mammary vessels were exposed and ligated on either side of the sternum in the fifth interspace; the sternum was transected at this level and the upper half was split using a Gigli saw, the two halves were spread, and the incision was carried down to the trachea itself. The whole area was embedded in extremely dense scar tissue. Running through the center of this fibrous mass, and intimately adherent to the front of the trachea, was the innominate artery. A most tedious dissection over many hours was necessary before the artery and the arch of the aorta were sufficiently freed from the trachea to expose the strictured area (Figure 2).

There was complete destruction of the tracheal anatomy and no tracheal rings were present in the 6 cms. or so above the carina. The tracheal lumen over and above the stricture site was opened, and the endotracheal tube was removed for a moment so that the stricture could be palpated more easily. Eventually, it was split with the finger, in the manner of a commissurotomy, and it was evident that a graft would be essential to close the defect.

A large elliptical full thickness skin graft was obtained from the outer side of the thigh, and a piece of tantalum gauze molded into a prosthesis which replaced the anterior three quarters of the trachea for the length of the stricture. The skin was then

folded in and around the tantalum gauze prosthesis and tacked to the gauze by interrupted sutures. The remaining fragments of stenosed trachea anteriorly were removed and the graft put in place and sutured in position by multiple chromic catgut sutures around the periphery of the defect. The lower edge of the graft was about 1 cm. from the carina. Before tying these sutures, the anesthetist passed an endotracheal tube of wire enforced latex down through the nose and past the graft so that it lay just above the carina (Figure 1).

Closure of the chest was performed in the usual way, and her condition at the conclusion of this procedure, which lasted nine hours and 35 minutes, was extremely good. She received 2500 cc's. of blood during the operation.

Over the next few days her general condition remained excellent and breathing through the nasal endotracheal tube was unobstructed. However, quite suddenly, on the fifth postoperative day, she had a sudden torrential hemorrhage and died almost instantly.

Autopsy revealed a small perforation in the posterior part of the innominate artery just opposite the point where it was in contact with the graft and where so much dissection had been necessary in order to free the artery.

The graft itself was in excellent shape and, apart from a small defect inferiorly due to detachment of two or three sutures nearest the carina which probably would not have given trouble if the hemorrhage had not occurred, there was no reason to suppose that the graft would not have taken. The tantalum gauze was covered over its whole area by the full thickness graft and was nowhere in contact with the artery. The hole in the artery must, therefore, have been due to operative trauma weakening the wall during the dissection.

Discussion

This case is presented because it emphasizes certain unusual difficulties and features of sequelae of tracheal trauma. The actual mechanism of the injury in such a case is not quite clear. Thompson and Eaton[1] believe it is related to a shearing force with a sudden increase in the intrathoracic pressure or to a sudden increase in this pressure with the glottis tightly closed. In cases where the moment of impact is anticipated, as in head-on auto wrecks, there is little doubt that reflex closure of the glottis occurs with consequent increase in intrathoracic pressure. In accidents where the blow is unexpected or the whole cycle of trauma occurs over an appreciable interval, however, it is difficult to believe that this is the invariable mechanism.

We believe the stricture in this case was due to severe crushing and destruction of the tracheal wall between the manubrium and the vertebral bodies. In an older person this would inevitably have resulted in a "stove in chest" with fractures of the ribs and sternum. Her youth, however, and the elasticity of the bony thorax were sufficient to withstand a sudden severe compression without bony injury.

One of us (C.F.A.C.) has in the past sustained a manubrio-sternal dislocation from a steering wheel injury—no fractures were present and the dislocation, which was complete, reduced itself in two days with posture alone. However, a severe tracheitis was present for a period after the injury, and it would seem likely that a similar but much milder injury to the trachea had occurred.

Another possibility suggested in this case was that the tracheal damage was a result of irritation from the end of the tracheostomy tube. But, in view of the gross tracheal destruction and the fact that we can find no such sequelae reported after the use of tracheostomy tubes, it seems to be unlikely.

A further point of interest is the involved area at the last bronchoscopy on December 13, 1955. Prior to this, the case had been discussed with

Jackson[23] who advised intensive antibiotic therapy. This was undoubtedly responsible for the disappearance of the granulation tissue and apparent healing of the stricture.

Exposure: The most suitable exposure was considered carefully before operation. Most of the recorded cases in a similar site have been approached through a high posterolateral incision in the face down position. There is little doubt, however, that the extreme fibrosis in this case would have added to the difficulties of exposure, as access to the tracheostomy stoma was essential so that the area around it could be excised. In retrospect, it was considered that the sternal splitting approach was most suitable, but even with this the carinal region was not easily accessible.

An important point of technique is the transection of the sternum and splitting of the upper half only. There is no doubt that this results in greater postoperative stability with consequent decrease in pain and more effective coughing.

Type of Prosthesis: When the dissection had been completed, the space between the posterior tracheal wall and the innominate artery was a mere slit, and it was evident that a fairly rigid prosthesis would be required. It did not seem that the method advised by Gebauer,[15] namely, wire supported dermal graft, would have been rigid enough to keep the lumen open; thus, the tantalum gauze was used instead.

Anesthesia: The importance of having an adequate variety of sterile endotracheal and endobronchial tubes available for direct insertion by the surgeon is emphasized. We had available two tubes connected to a Y piece which could, if necessary, have been inserted into the main bronchi if the stricture was right against the carina. Luckily, this did not occur.

A bronchoscope set up and ready before anesthetic induction is essential and undoubtedly saved this patient's life, albeit temporarily.

Rapidity of Stricture Formation: The most obvious conclusion to be drawn from this case is that once a tracheal stricture of this degree has developed, no amount of conservative treatment will be effective and definitive resection is mandatory. The apparent healing of the stricture and smoothness of the wall on bronchoscopy is deceptive and, if left unsupported, will inevitably stenose.

ADDENDUM

Since the submission of this paper, Keshishian, Blades, and Beattie have published in the J. Thoracic Surg., 32:707, 1956, an excellent article on tracheal reconstruction.

SUMMARY

1. Rupture or laceration of the trachea, particularly if accompanied by any tissue destruction, is nearly always followed by stricture formation.

2. The various methods and techniques for dealing with such a stricture are discussed. The best results have been obtained when the rigidity was maintained by some latticed or open work prosthesis, allowing granu-

lation tissue extrusion through the gaps and subsequent epithelialization within the lumen.

3. Dilatation and intensive antibiotic therapy may give apparent improvement in the bronchoscopic appearance, but the disappearance of granulation tissue is deceptive. The rapidity of stricture reformation is emphasized.

4. The case reported is of a young married woman with an almost complete stricture of the trachea, 6 cms. in length, just above the carina. This was the sequel to severe chest trauma.

5. The treatment was by resection of the stricture and subsequent replacement by a dermal graft reinforced by tantalum gauze.

6. Exposure problems and the anesthetic technique are discussed. Transection of the mid sternum with splitting of the upper half is a satisfactory approach.

7. It is concluded that conservative treatment of such a case is ineffective and surgery is therefore mandatory.

RESUMEN

1. La ruptura o laceración de la tráquea, especialmente si se acompaña de destrucción de tejido, casi siempre es seguida de estenosis.

2. Se discuten los diversos métodos y técnicas para tratar tal estenosis. Los mejores resultados se han obtenido cuando la rigidez se mantuvo por alguna prótesis abierta o enrejada que permita la protrusión de tejido de granulación a través de sus aberturas y así la epitelización del lúmen.

3. La dilatación y la terapéutica con antibióticos, pueden dar aparente mejoría según los aspectos broncoscópicos con la desaparición del tejido de granulación, pero esto es engañoso. La rapidez de la formación de la estenosis se recalca.

4. El caso que se presenta es de una mujer casada con uná estenosis casi completa de la tráquea en 6 cms. de extensión justamente arriba de la carina como consecuencia de un trauma de tórax.

5. El tratamiento fué la resección de la estenosis y la substitución por un injerto dérmico reforzado con gasa de tantalio.

6. Se discuten los problemas de la exposición y la técnica de la anestesia. La transección a la mitad del esternón con división de la mitad superior del mismo, es una técnica satisfactoria para abordar la tráquea.

7. Se concluye que el tratamiento conservador en tal caso, no es efectivo y que es imperioso recurrir a la cirugia.

RESUME

1. Une rupture ou une plaie de la trachée est à peu près toujours suivie par un processus de sténose, surtout s'il y a une part de destruction tissulaire.

2. Les auteurs discutent les différentes méthodes et techniques qui peuvent empêcher cette évolution. Les meilleurs résultats ont été obtenus quand la rigidité a pu être maintenue grâce à une prothèse tissée qui per-

met au tissu de granulation de faire issue à travers les orifices et entraine une épithélialisation de l'intérieur du conduit.

3. La dilatation associée à un traitement antibiotique intensif peut donner une amélioration apparente qui se traduit bronchoscopiquement par la disparition du tissu de granulation. Mais les résultats sont alors décevants. Les auteurs insistent sur la rapidité avec laquelle se reconstitue la sténose.

4. Ils rapportent l'observation d'une femme jeune mariée qui était atteinte d'une sténose presque complète de la trachée située juste au-dessus de la carène et consécutive à un grave traumatisme thoracique.

5. Le traitement consista en la résection de la sténose et son remplacement par une greffe dermique renforcée par un filet de "tantalum."

6. Les problèmes de la voie d'abord et de l'anesthésie sont mis en discussion. La section du sternum en son milieu avec division de la moitié supérieure de l'os est une voie d'abord satisfaisante.

7. La conclusion des auteurs est que dans de tels cas le traitement conservatif est inefficace et que par conséquent le traitement chirurgical s'impose.

ZUSAMMENFASSUNG

1. Einer Ruptur oder Verletzung der Trachea, besonders wenn sie von irgend welcher Gewebszerstörung begleitet ist, folgt so gut wie immer die Bildung einer Striktur.

2. Die verschiedenen Methoden und Techniken zur Behandlung einer solchen Striktur werden erörtert. Die besten Ergebnisse wurden dann erzielt, wenn die Starre aufrecht erhalten wurde durch eine gegitterte oder offene Prothese, die dem Granulationsgewebe den Vorstoss durch die Lücke mit nachfolgender Epithelialisierung innerhalb des Lumens ermöglichte.

3. Dehnung und intensive antibiotische Therapie können im bronchoskopischen Erscheinungsbild zu einer augenscheinlichen Besserung führen mit Rückbildung des Granulationsgewebes; aber dies ist trügerisch. Die Schnelligkeit des Wiederauftretens der Striktur wird betont.

4. Der Fall, über den berichtet wird, ist der einer jungen verheirateten Frau mit einer fast kompletten Striktur der Trachea von 6 cm Länge, gerade oberhalb der Carina, die die Folge eines schweren Brustkorb-Traumas war.

5. Die Behandlung bestand in einer Resektion der Striktur, die ersetzt wurde durch eine mit Tantal-Gaze verstärkte Hautplastik.

6. Die Probleme der Freilegung sowie die Technik der Anaestesie werden erörtert. Ein Querschnitt der Mitte des Sternums mit Spaltung der oberen Hälfte ist der befriedigende Zugang.

7. Es wird die Folgerung gezogen, dass konservative Behandlung eines solchen Falles wirkungslos ist und chirurgisches Vorgehen unerlässlich.

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Tuberculosis in Various Ages and Different Races: Anachronisms*

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To have the privilege of presenting the 1956 Varrier-Jones Memorial Lecture here, where, within a relatively short radius nearly all of the fundamental inventions and discoveries in tuberculosis were made, is a most significant honor.

With a disease of such antiquity, so widespread and so destructive among people and animals, it was to have been expected that various methods of dealing with the new armamentarium would develop among people in different parts of the world or even in the same nation. Such factors as their improper use, misinterpretations, conclusions drawn from insufficient evidence, formulation of theories, expression of personal opinions, etc., were sure to complicate the problem and mislead workers, thus seriously retarding progress. All of these and more have occurred to such a degree as to cause much confusion. It is particularly fitting that physicians in diseases of the chest from around the world should gather here and evaluate the procedures employed in the past and to recommend abandonment of anachronisms.

Longitudinal Observations

In 1920 vantage ground was provided for observations on tuberculosis in people which has been occupied to this time. From this position, persons of all ages, from birth to death in senility, infected and uninfected with tubercle bacilli, sick and well, engaged in numerous occupations, etc., have been observed. In 1920 and subsequently, views were expressed with reference to varying effects of tuberculous infection acquired at different ages in life of both people and animals.

When it was observed that the adult guinea pig, like the human infant, has a high percentage of lymphocytes, whereas the newborn guinea pig has a low lymphocyte count, similar to that of adult humans, it was thought this might account for the alleged low resistance of young guinea pigs to tubercle bacilli. Various theories and expressions of opinion led Krause[1] to make the following statement in 1925: "Because paper after paper of those appearing on many subjects in tuberculosis avers that young animals are in general inordinately susceptible to tuberculosis and because many an

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author easily and lightly solves a knotty problem as it arises with the statement of the assumption, it is particularly desirable to point out on how slender a basis of ascertained fact the assumption is based." This led him to undertake a study of resistance of young and old guinea pigs. His experiments revealed that when young and old guinea pigs are infected intracutaneously with relatively small quantities of virulent tubercle bacilli that are equal for all the animals, there is an earlier appearance and more vigorous development of tubercles at the site of inoculation than in the regional lymph nodes in the old animals. "After infection of this nature and heavy enough to cause generalized tuberculosis in the old animals, both young and old guinea pigs developed essentially the same grade of infection. There was nothing to indicate that the young were more susceptible than the old."

When he infected subcutaneously with large quantities of virulent tubercle bacilli in equal dosage, a more extensive and progressive involvement resulted in the young than in the old animals. Inasmuch as the young animals received double the quantity of tubercle bacilli per body weight that was sufficient to cause fatal disease in the old animals, he believed the more advanced condition found in the young animals was a result of overdosage.

Veterinarians also found no evidence of low resistance among young domestic animals.

Infancy and Early Childhood

In 1920 many persons had expressed the opinion that in infancy and early childhood the human body has exceedingly low resistance to tubercle bacilli. However, search of the literature revealed that practically all that had been said and written was a matter of opinion since no well documented study had been made to justify a conclusion. Reports in the literature already available and many subsequently made were based upon mortality among children with reinfection clinical type of tuberculosis. These included such conditions as meningitis, miliary disease and pneumonia, which were nearly always fatal, as well as clinical lesions in peripheral lymph nodes, bones, joints, etc., from which children usually do not die. Both of these acute and chronic forms of tuberculosis are now known to be reinfection type. They are always preceded by primary disease which rarely causes significant symptoms but results in endogenous reinfections.

In series of cases reported rarely has there been an attempt to determine how many infants and young children had been infected with tubercle bacilli in the areas from which the ill ones originated. Therefore, nothing was known of what percentage of infected infants developed reinfection type of tuberculosis.

Krause[2] said, "The more I see of tuberculosis in infants and the more I confirm diagnosis by the aid of new methods, the more tuberculous infants I find who run along with comparatively little illness and withstand their infection well."

Inasmuch as only a few years constitute this period of life and since many children were being infected, it was possible from our vantage

ground to determine the immediate results of primary infection rather promptly.

Between May, 1921 and November, 1941 we examined 5,537 children from birth to five years of age, of whom 831 reacted to tuberculin (18 could not be completely examined; therefore, only 813 were considered).[3] Among these 813 children, 102 (12.54 per cent) presented primary infiltrates which subsided in the usual manner without causing significant illness. Eleven (1.35 per cent) developed acute fatal reinfection forms of disease, of whom two had tuberculous pneumonia, four meningitis, and five generalized miliary disease. Eleven (1.35 per cent) other children among the 813 developed reinfection chronic type of tuberculosis in bones, joints, lymph nodes, etc.

Among the nonreactors in the group of 5,537 children from birth to five years of age, 198 were subsequently found to be reactors, two of whom died from meningitis and one from tuberculous pneumonia. Two others developed tuberculosis of bones and joints, and three chronic pulmonary lesions. Thus, the toll in illness and death among 1,011 children was 30 (2.96 per cent). The other infected children (97.04 per cent) remained free from clinical tuberculosis during the period of childhood. Had only the children with clinical disease been studied, 14 (46.7 per cent) who died would have given an erroneous impression of the ability of infants and young children to control tubercle bacilli.

For too long we talked about "high susceptibility" and "low resistance" and theorized about methods of inceasing resistance to tubercle bacilli when such factors as intimate contact exposure should have claimed our greatest attention. Infants are often subjected to excessive fondling and kissing by members of the immediate families as well as relatives, including grandparents. Elderly neighbors also participate in this activity.

Infants and young children are endowed with an exceedingly efficacious defense mechanism against first invasions with tubercle bacilli as manifested by the relatively few who develop reinfection type of lesions and succumb soon after becoming infected.

From the age of about five years until adolescence, chronic clinical primary tuberculosis rarely occurs among girls and boys. In the earlier years of this period, of the clinical lesions which do develop, a preponderance are extrathoracically located. Over a 20 year period[3] beginning in 1921, we examined 6,823 children, from six to 14 years of age on the first visit, of whom 2,979 reacted to tuberculin. Of this number, 137 (4.6 per cent) had reinfection type of tuberculosis when first seen or subsequently developed it. Thus the morbidity rate was higher in this age period than among infants and young children, but their extrathoracic lesions were less fatal. Nevertheless, the low mortality rate in this age period has been attributed theoretically to operation of special resistance. It may be of considerable importance that at this time of life many girls and boys resent fondling. There is a strong tendency for them to engage in separate activities, such as participation in games, parties, etc. Wherever they are assembled, including school, rarely do girls or boys become infected from others of their age.

Teens and Early Twenties

Chronic pulmonary tuberculosis makes its debut as adolescence approaches and has often been reported as prevalent and highly destructive during the teen ages and early 20's. Lowered resistance during this period has been given most attention. Although no indisputable proof has been adduced, numerous factors have been thought to contribute to lowering of resistance, particularly among girls, such as sex hormones, scanty wearing apparel, diet fads, fatigue, etc.

We have previously reported observations on the effects of tuberculous infection acquired among children and adolescents which did not show that the latter are more susceptible to infection than persons in other age periods.[3] The reason for chronic pulmonary tuberculosis making its debut in or immediately preceding adolescence and continuing throughout the decades of life has not been satisfactorily explained.

It would appear that the important factors have been largely overlooked. First, in areas where considerable contagion exists, there has been an accruement of primary tuberculosis from which endogenous reinfections now result in clinical disease. Second, this is the mating period of life. It is when girls and boys assemble in small and large groups with intimate contact. Parents often advise their daughters to have numerous men associates in order to choose the most desirable life mate and vice versa. Thus, a single teen-age girl or boy with contagious tuberculosis may infect many others. Contact exposure occurring outside the home is an extremely important factor. This is the period in life when people are "on the move" more than any other. Downes has shown that approximately 66 per cent of persons who developed tuberculosis in the community under her observation had contracted it from sources outside their families.

Prostitution probably is in vogue to greater extent in this period of life than any other. In one country said to have 1,200 licensed houses of prostitution, a survey of 1,300 inmates revealed that 10 per cent had active pulmonary tuberculosis.[4]

The belief often expressed that clinical pulmonary lesions are more severe and more prevalent in adolescence probably is in part due to failure to differentiate between primary infiltrates (Ghon tubercles) and clinical reinfection type of lesions. Too often, when extensive disease is found in an adolescent on first examination, it has been assumed that the infection was of recent origin. There had been no periodic tuberculin testing, and there was no way of knowing when the infection actually occurred.

In 1916 when 70 per cent of grade-school children in the city of Minneapolis reacted to tuberculin, 268 girls and boys, ages 10 to 19 years, died from tuberculosis in Minnesota, whereas in 1955, when 4 per cent of grade-school children reacted, only one died in the teen-age period (Figure 1).

When in the third decade of this century, special attention was called to the seriousness of tuberculosis among students and recent graduates in nursing in that they developed much more clinical tuberculosis than women or men of the same age in the general population, there were those who stoutly maintained that age of the students was the deciding factor. It

was said that they were in that age period when resistance to tuberculosis is exceedingly low, and the problem could be solved only by admitting older persons to our schools of nursing. Time has proved it was not the age of the students but contagion to which they were subjected that created the problem.[5]

The prevalence of the disease in clinical form during the teen-age period apparently is dependent upon incidence of infection. We have not seen a relatively higher percentage of infected persons at this age develop clinical lesions than in later life.

The many new infections acquired during the teen ages and early 20's together with those obtained in pre-adolescence are sufficient to account for the surge of clinical cases in adolescence and thereafter.

Later Life

Following marriage, the previous excessive exposure rate tends to subside because of the decrease in the number of intimate contacts. However, in many areas by this time a high percentage and in some places all are harboring tubercle bacilli, and reinfection clinical types of disease

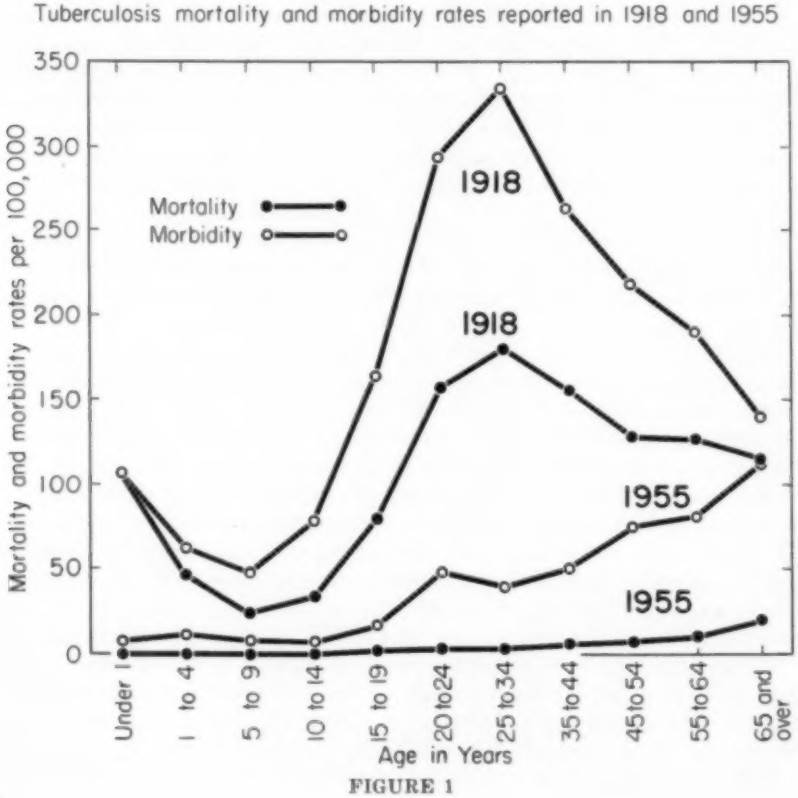

FIGURE 1

continue to appear among them, increasing through the decades of life.

During the last two or three decades, in parts of the world where good tuberculosis control programs have been in effect, there has been a marked reduction in infections acquired in childhood and early adult life, with correspondingly reduced morbidity and mortality. However, in the upper age brackets, morbidity and mortality have continued high, so much so that tuberculosis has been designated a disease of older people. Here again, it has been contended that this situation is due to lessened resistance among elderly people. In reality, this older age group is composed of individuals, a large percentage of whom acquired tubercle bacilli in early life which they have continued to harbor and which are endogenously causing reinfections.[6]

Observations on Persons Infected in Adulthood

Since 1920 we have seen 2,315 persons who became infected with tubercle bacilli so as to convert from nonreactors to reactors to tuberculin at the age of 19 years and older. Deducting 34 who were not recently traced, there were 2,281 for consideration. Of this number, 15 had died. They had 199 person years of follow-up with no evidence of clinical tuberculosis having developed.

Among the remaining 2,266 there are 2,080 with 24,431 person years of follow-up who have developed no demonstrable tuberculous lesion (Table I).

Among the remaining, there were 54 with primary infiltrates (Ghon tubercles in the inflammatory stage) of such size, consistency and location as to cast visible x-ray shadows. They have had 749 person years of follow-up.

Another group of 67 developed pleurisy with effusion, of whom nine had co-existing primary pulmonary infiltrates. They have had 932 person years of follow-up.

TABLE I—FOLLOW-UP FINDINGS ON 2,266 PERSONS WHO BECAME INFECTED WITH TUBERCLE BACILLI IN ADULTHOOD

Age Infected	Number	Normal X-ray Films	Primary Infiltrates	Pleural Effusion	Clinical		Person Years of Follow-up
					Pulmonary	Extra-Pul.	
19	86	85	0	0	1	0	969
20	167	157	4	3	3	0	2173
21	272	241	7	13	10	1	3810
22	278	248	9	10	11	0	4179
23	191	177	1	5	8	0	2688
24	217	194	7	7	9	0	3290
25	168	155	5	4	3	1	2438
26 - 30	474	428	16	19	10	1	5455
31 - 35	211	200	2	4	3	2	1345
36 - 40	103	97	3	2	1	0	499
41 - 49	99	98	0	0	1	0	253
TOTAL	2266	2080	54	67	60	5	27,099

A third group consists of 65 who presented clinical reinfection type of tuberculosis, of whom five were extrathoracic lesions and 60 were pulmonary. They have had 987 person years of follow-up.

Thus, there have been 27,099 person years of follow-up for the 2,266 converters.

Primary Infiltrates (Ghon Tubercles)

In the entire group, (Table II) 54 presented primary infiltrates of sufficient size, density, and so located that their shadows were visualized on x-ray film. No other evidence of disease was seen. These were classified as primary infiltrates because they appeared about the time allergy could first be demonstrated, and because their subsequent course was typical. These persons have been observed from two to 25 years since the primary infiltrates were first seen, a total of 749 person years of follow-up (Table II). Throughout this period, five (9.3 per cent) subsequently developed clinical tuberculosis. One with primary lesion in evidence in 1931 had reinfection type of disease in 1941. One became a tuberculin reactor and primary infiltrate was present in April, 1931. In August of the same year he had tuberculous epididymitis, in February, 1932, tuberculous peritonitis, in April, 1937, involvement of one of the bones of the right foot, and in 1946, tuberculosis of a kidney required nephrectomy. Another who had primay infiltrate in 1932 had reinfection type of disease in 1934. One with primary infiltrate in 1945 had reinfection pulmonary lesion in 1948. One whose primary infiltrate was in evidence in 1948 had reinfection type of tuberculosis requiring treatment in 1949 and again in 1953. The remaining 49 individuals with demonstrable primary infiltrates have shown no evidence of clinical tuberculosis.

Pleurisy with Effusion

This is an allergic reaction and most often is caused by sub-pleural pulmonary lesions which extend into the pleura. Many of the cases occur

TABLE II—DEMONSTRABLE PRIMARY PULMONARY INFILTRATES AMONG 2,266 PERSONS INFECTED IN ADULTHOOD

Age When Infection Occurred	Number of Adult Converters	Number of Demonstrable Infiltrates	Number with Subsequent Clinical Lesions	Total Years of Follow-up After Infection
20	167	4	2	47
21	272	7	1	72
22	278	9	1	167
23	191	1		4
24	217	7	1	119
25	168	5		85
26 - 30	474	16		216
31 - 35	211	2		14
36 - 40	103	3		25
TOTAL	2081	54	5	749

about the time allergy is first detectable by the tuberculin reaction. In fact, pleurisy with effusion, with its usual sudden onset, is often the first manifestation that the individual has been infected. Among the entire group of tuberculin converters traced, 67 developed pleurisy with effusion, of whom 14 had coexisting demonstrable primary pulmonary infiltrates. They have had a follow-up of 932 person years (Table III). In all but four, the effusion appeared within a few months to one year after the tissues were sensitized to tuberculo-protein. One who was infected in 1933 did not have effusion until 1951. Another had effusion two years after infection. In one, infection occurred in 1940 and the effusion in 1948. The fourth was infected in 1933 and effusion developed two years later.

Nine (13.4 per cent) of the 67 have developed clinical tuberculosis. One infected in 1932 had effusion in 1936 and pulmonary tuberculosis in 1942. One with effusion in 1932 had tuberculous pneumonia in 1933 and died from pulmonary hemorrhage in 1936. One had pleurisy with effusion in 1933 and minimal reinfection pulmonary disease in 1935. One was infected in 1940 and had pleurisy with effusion in 1948, coexistent with disease in the uterus, uterine tubes, and one ovary. One with pleurisy with effusion in 1940 had pulmonary tuberculosis in 1946. One whose effusion appeared in 1941 had pulmonary tuberculosis in 1942. One had effusion in 1945 and bilateral pulmonary tuberculosis moderately advanced a year later. One who had pleurisy with effusion in 1947 had co-existing tuberculous peritonitis. One with effusion in 1949 had tuberculosis of pelvic organs and peritonitis in 1953.

Among these nine persons who had pleurisy with effusion and developed clinical lesions, two had primary pulmonary infiltrates in evidence when effusion was present. These nine persons have had 187 person years of follow-up.

TABLE III—PLEURISY WITH EFFUSION AMONG 2,266 PERSONS INFECTED IN ADULTHOOD

Age When Infection Occurred	Number of Adult Converters	Number of Cases	Subsequent Lesions	Total Years of Follow-up After Pleurisy
20	167	3	1	43
21	272	13		175
22	278	10	1	146
23	191	5		91
24	217	7	2	93
25	168	4	1	61
26 - 30	474	19	3	263
31 - 35	211	4	1	35
36 - 40	103	2		25
TOTAL	2081	67	9	932

Clinical Tuberculous Lesions

In addition to the converters who had primary infiltrates and those with pleural effusion, there were 65 who developed clinical lesions, of which 60 were pulmonary and five extrathoracic. These 65 had 987 person years of follow-up (Table IV).

It is possible that a few primary infiltrates were classified as reinfection type of lesions, because after graduation, in these particular cases, the tuberculin testing intervals were too long for accurate classification.

In 34 of the 65, the clinical lesions were in evidence within the first two years after the infection occurred. In the remaining 31, they appeared three or more years after tuberculin conversion. In fact, in seven it was 10 years or more, including three in whom 18 years elapsed.

Death occurred in two cases not included in Table IV because the time of initial infection was not known. One who graduated from a school of nursing as a nonreactor to tuberculin in 1937 died from pulmonary tuberculosis in a sanatorium in 1942 at the age of 27 years. The institution's records were destroyed, and it was not known when she became infected. The other graduated from a school of nursing in 1943 as a nonreactor to tuberculin. In 1947, at the age of 25 years, she died from tuberculous meningitis, but no tuberculin test was administered after graduation.

Another student of nursing (not included in Table IV for the same reason) who graduated as a nonreactor to tuberculin in 1931 was found to have extensive pulmonary tuberculosis in 1948. Although she had worked in a sanatorium, no tuberculin test had been administered in the interim because, "I don't believe in tuberculin tests but have had periodic x-ray films of my chest."

A medical student whose previous tuberculin tests had been negative was found to be a reactor in February, 1935. The next month he had ery-

TABLE IV—CLINICAL TUBERCULOSIS AMONG 2,266 PERSONS INFECTED IN ADULTHOOD

Age When Infection Occurred	Number of Adult Converters	Number of Cases		Total Years of Follow-up Since Infected
		Pulmonary	Extrathoracic	
19	86	1		20
20	167	3		61
21	272	10	1	204
22	278	11		168
23	191	8		116
24	217	9		135
25	168	3	1	48
26 - 30	474	10	1	165
31 - 35	211	3	2	52
36 - 40	103	1		8
41 - 49	99	1		10
TOTAL	2266	60	5	987

thema nodosum. Approximately two years later, tuberculosis was found in a costal cartilage. Over the next few years, he had lesions appear in the lumbar spine and one hip joint, from which he made good recoveries.

One nurse 14 years after graduation (1944) developed bilateral pulmonary sarcoidosis. Subsequently she was in a sanatorium for brief periods in 1944 and 1946. In 1948 she was found to be a reactor to tuberculin and a diagnosis of pulmonary tuberculosis was made.

Throughout these observations we have seen no difference in the types of lesions which developed or their subsequent behavior among persons whose initial infections were acquired in adulthood and those whose infections occurred earlier in life. Primary pulmonary infiltrates, which are Ghon tubercles in the inflammatory stage, took the same general course of regression and were just as benign as those we have often seen in children. The rapidly progressive and highly fatal primary disease, sometimes spoken of as the "infantile type," was not seen in any person who became infected in adulthood.

Among these 2,266 persons who first became infected in adulthood we have seen only two cases of tuberculous pneumonia. Each one occurred several years after the initial invasion. There has been but one case of meningitis and no miliary disease.

Those among the adult converters who had pleurisy with effusion were no different in immediate severity or subsequent developments than one sees among those infected earlier in life.

There were 65 persons who became infected as adults who did not have demonstrable primary infiltrates or pleurisy with effusion but developed clinical tuberculous lesions. These lesions were no more extensive or difficult to manage than those which we have seen develop in individuals of the same age but who had carried their infections since childhood. In a study on tuberculosis in physicians, we found that a larger number (3.6 per cent) of clinical lesions appeared among those who had been infected before entering medical school than among those (2.2 per cent) who became infected while in school or later.[6a] Similar figures were observed among nurses.[5] The logical explanation appears to be that among those who were infected earlier in life, the disease has had more time to mature than among those infected later. We have seen no evidence to indicate that age of the individual when the infection occurred played a significant role.

It is exceedingly encouraging that persons who become infected as adults possess the same effective defense mechanism as children. Therefore, the longer the initial invasion is postponed, the less of life's span remains for clinical lesions to mature.

The statement so often made that most clinical tuberculosis develops within two years after the initial infection occurs is probably the result of deductions being drawn from far too short periods of observation. While it is true that 34 of the 65 clinical cases observed in this study occurred within two years after the initial invasion, the remaining 31 cases evolved from three to 18 years after the primary infection occurred. All of the cases that could develop within two years after infection are now on record, but

new clinical cases continue to develop in this group of 2,269 who became infected in adulthood. If new lesions evolve at the usual rate, those that appear more than two years following the initial invasion will soon surpass those which appeared during the first two years.

Tuberculosis is a lifetime disease, and it is well known that clinical lesions may appear soon after the invasion occurs or at any subsequent time including senility. In parts of the world where children and young adults have been well protected against tubercle bacilli, most of the morbidity and mortality is now occurring among persons in the upper age brackets. There is good historical and postmortem evidence that many of these older persons have carried their infections since childhood and are developing clinical lesions decades later. There is no reason to suspect that this will not occur among some of those reported here as they reach the upper age backets.

Race and Nationality

The belief that different races and nationalities of people possess varying degrees of susceptibility and resistance to tubercle bacilli is no longer tenable. The Jewish race was placed at one extreme, with the Negro and the American Indian at the other. The deciding factor was thought to be resistance which was believed to vary enormously in the different groups of people of the world.

To date, no well documented evidence has been found to show that Jews at any time or anywhere have manifested an innate resistance to tuberculosis different from that of other people under the same conditions. There is evidence, however, that in general Jews have not suffered as much from tuberculosis as some people of other races and nationalities. Probably this is because Jews have been protected against tubercle bacilli since the Mosaic laws prohibited the use of flesh as food from animals suffering from consumption. Moore says: "The Mosaic laws (Leviticus xxii, 22) contain rules that the flesh of animals which suffer from "wen or scurvy" should not be used as food. The Talmud, especially the Mishnah, codified at the close of the second century, and the Gemara (fifth century) contain numerous enactments against the eating of such flesh. It is stated on good authority that 'kandi' and 'timari' refer to tuberculosis." The well-known, long-standing hygienic practices of Jews, such as washing hands before eating, have been a deterrent against tubercle bacilli. When brought in contact unavoidably with tubercle bacilli, Jews develop benign primary tuberculosis and are as likely later to have reinfection clinical disease as other peoples.

The American Indian and Negro, long pointed to as having such high susceptibility and low resistance, have lived under diametrically opposite conditions. Krause[7] says: "Out of a single fact numerous writers have built up a rather stiff doctrine that avers an exceptional lack of innate resistance of primitive peoples to tuberculosis. The basic fact is the common observation that the introduction of tuberculosis among less civilized populations is followed by excessive mortality, the result of comparatively acute illness. The fact is conceded; the conclusion stated is not denied;

yet it is submitted that it need not follow from the premise; and it is maintained that the premise does not prove it."

"And it is suggested that circumstances other than innate lack of resistance, circumstances too that are facts, may contribute toward rendering tuberculosis unusually destructive and fatal for those of low civilizations—at any rate, for those who come in contact with the whites of Europe and America."

"Judged by our standards, the common living habits of savages and semi-savages are inordinately dirty. At any rate, they are supremely adapted to the contracting and spread of bacterial diseases, particularly one like tuberculosis, unique among infections in that it can be contracted in every conceivable way, via every possible portal of entry, directly and through an intermediary carrier. The common bowl without individual utensils at meals; the intimate herding at sleep; the windowless, chimneyless, never cleaned, littered habitations, if dwellings there are; the unwashed, oiled and pomaded bodies or the filthy rags if clothes are worn, must individually and together be regarded as hothouses of infection, if tubercle bacilli are loose. We cannot imagine a more fertile soil in which to spread an infection; as for tuberculosis, all that is needed is the sowing of the bacillus. And if seed-time ever does come, it will be marked by extreme dissemination and quantity of germs."

A quarter of a century ago, mortality and morbidity were so high among American Indians that it was often said tuberculosis would annihilate the race. This fatalistic point of view was based on the supposed inability of the Indian's body to cope with tubercle bacilli. Although much had been done by way of providing sanatoriums and treatment with marked success among Caucasians, nothing whatsoever had been offered the Indians on their reservations. For example, in the state of Minnesota, no provision had been made to protect the Indian population against those who had contagious tuberculosis. Those who died did so among their people, to whom they had disseminated tubercle bacilli. Tuberculin testing in 1931 revealed that 15.3 per cent of the white children reacted while 40 per cent of pre-school-age and over 65 per cent of school-age Indian children in the same county reacted to tuberculin. In 1937, the tuberculosis mortality rate was 529.2 per 100,000 population among Indians but only 33.5 among Caucasians. In 1934, a sanatorium with 117 beds for Indians was opened. Other measures were introduced which had long been in practice for Caucasians. The tuberculosis mortality rate among Indians decreased sharply after 1937, but was interrupted in 1943-44 because of lack of funds to adequately operate the sanatorium. Thereafter, it decreased, and in 1955 no Minnesota Indian died from tuberculosis (Figure 2). This is convincing evidence that it was not a matter of the Indian's susceptibility or resistance to tubercle bacilli but rather one of contagion, which yielded promptly when vigorously attacked. Moreover, the incidence of tuberculin reactors among Indian school children has been reduced to approximately 5 per cent. Those in charge of management, including treatment, of tuberculous Indians

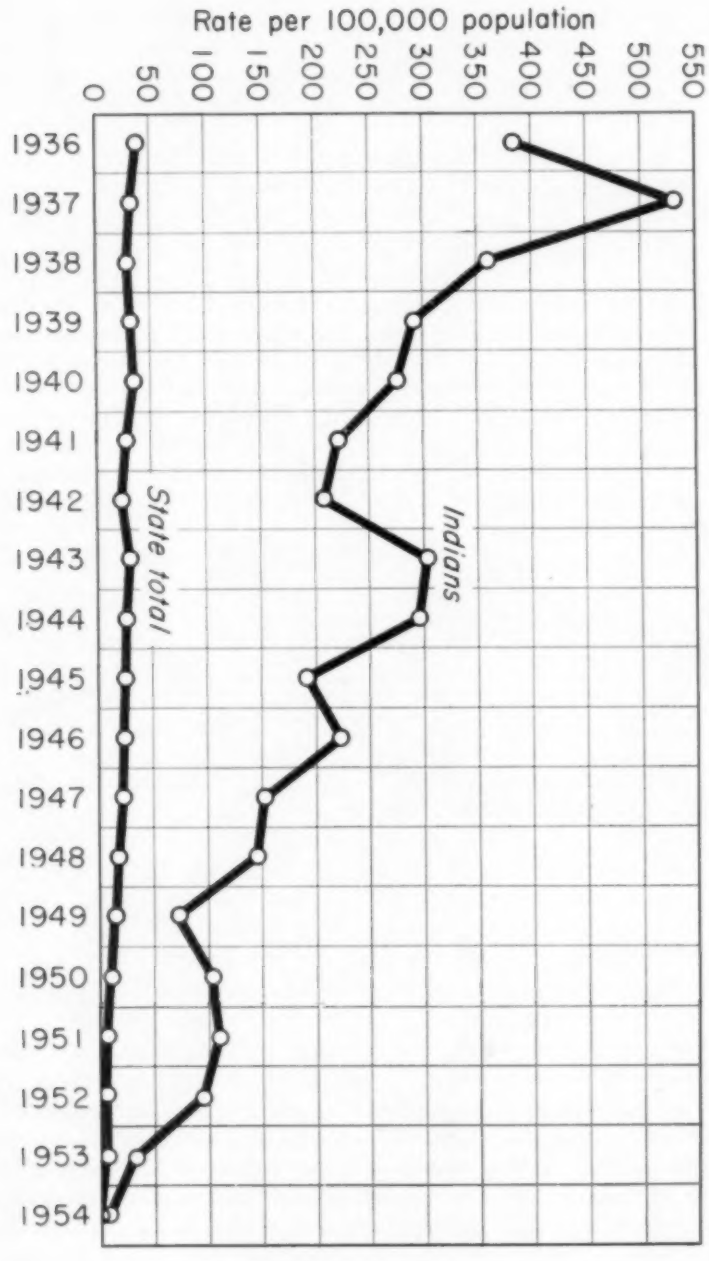
Rate per 100,000 population
0
50
100
150
200
250
300
350
400
450
500
550
1936
1937
1938
1939
1940
1941
1942
1943
1944
1945
1946
1947
1948
1949
1950
1951
1952
1953
1954
State total
Indians

FIGURE 2

reported that they responded to all forms of treatment in the same manner as Caucasians.

While conducting a tuberculosis survey on the Fort Peck Reservation in Montana in 1931, it was observed that three times as many Indian as white children reacted to tuberculin with a correspondingly high number of clinical cases.[8] However, no difference was observed between the white and Indian response to the infection. Lesions in the two races appeared identical, and the course they took was the same.

There is no well documented evidence to support the idea that the American Negro has suffered such devastation from tuberculosis because of high susceptibility or lack of resistance. Just as with the American Indian, tubercle bacilli were allowed to prey upon him for some time after good control measures had been instituted and practiced among Caucasians. Thus, tuberculous Negroes remained in their homes and communities to disseminate tubercle bacilli to others, many of whom in due time followed the same contagious course.

Wherever Negroes have lived under social conditions comparable to those of Caucasians, the tuberculosis problem has been essentially the same in the two races.

It has been pointed out that among Negroes there is a tendency to tolerate the disease without examination or treatment much longer than is true of Caucasians. Therefore, when they do report, Negroes are more likely to have advanced and fatal tuberculosis. Negro children respond to primary tuberculosis invasions in the same manner as white children.

In 1931, Bogen[9] reported on 4,730 patients admitted to the Olive View Sanatorium in Los Angeles. During the previous decade, more than one-half of the Negroes admitted had already died from tuberculosis, while only one-fourth of the Jews had died. On analysis of data, however, the reason was clear. The stage of disease at the time of admission to the sanatorium varied just as widely as did the mortality figures and generally in the same direction. More than three-fourths of the Negro patients were in the far-advanced stage on admission as compared to less than one-third of the Jews. More than half of all the patients in the sanatorium with far-advanced disease died during this period, less than one-fourth of those with moderately advanced, and only 3 per cent of those with minimal disease had succumbed. "This fact alone accounts for the wide apparent disparity in the death rates of the different nationalities."

There is no evidence to support the idea that special racial or national resistance is acquired by reason of tuberculosis having existed among the people for many decades or even centuries. If this were a reality, one would not expect that today the highest morbidity and mortality rates obtain in those nations where tuberculosis has been known to be rife for so many centuries. Or is there good evidence that tuberculosis in a family for several generations enables the present generation to fight off the disease better than in those families where there has been no tuberculosis for many generations.

It is well known that animal species vary in susceptibility and resistance.[8]

For example, human type of tubercle bacilli multiply and produce disease rapidly in the bodies of guinea pigs, whereas they cause relatively little disturbance in rabbits and, especially, rats. Apparently, this observed difference in species of lower animals is partially responsible for the belief that people of various races and nationalities differed in a similar manner. The fact was overlooked that human races belong to a single species.

Resistance Among the Mentally Ill

When so much tuberculosis was seen among persons in institutions for the mentally ill, the concept was advanced that mental illness lowers resistance. Apparently, this was generally accepted, and it was thought futile to attempt to solve the problem because so much mental illness was permanent. Late in the 19th century, Bracken[10] pointed out that the prevalence of tuberculosis among institutionalized patients was solely a matter of contagion. Persons with mental aberrations were being sent to these institutions with total disregard for possible co-existing contagious tuberculosis. So many were admitted with this disease and so many acquired a from them that such hospitals became infested with tubercle bacilli.

In Great Britain during World War I, there was increase in tuberculosis mortality among patients in hospitals for the mentally ill. In fact, between 1910 and 1914, it varied between 15 and 17 per 1,000 resident patients. During the war, however, it rose to 37 per 1,000 in 1917 and to 52 in 1918. By 1923 the rate had fallen to 10 per 1,000. Early in World War II, there was also an increase in the tuberculosis mortality in such institutions. In fact, in the institutions for the mentally deficient of England and Wales the tuberculosis death rate in 1941 exceeded that of 1937-39 by 80 per cent for men and 73 per cent for women.

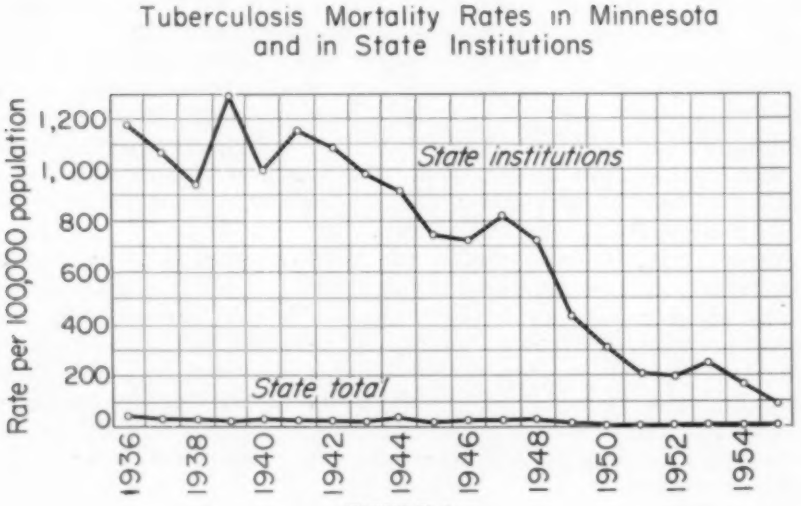

FIGURE 3

The increase in tuberculosis mortality in the institutions for the mentally ill in World War I was ascribed mainly to insufficient diet. However, the Committee on Tuberculosis in Wartime of the Medical Research Council of Great Britain reported in 1942 that it was not so much of that opinion.[11] This committee pointed out that a great deal of attention had been paid to both the quality and quantity of food provided these patients in World War II. Apparently, the increase was due to dissemination of tubercle bacilli resulting from overcrowding in these institutions. Blackouts reduced ventilation and many of the patients were unable to control cough and expectoration.

Thus, the low resistance concept prevailed until recently when the lack of resistance factor was discarded and the attack was made on the tubercle bacillus. Wherever this has been well done, tuberculosis among inmates of institutions for the mentally ill has declined precipitously (Figure 3). However, because the attack was started so late in such institutions, the disease has not yet been reduced to the same low level as in the general populations of the same areas. Moreover, there remains a large residual of infected older permanent residents among whom clinical disease will continue to evolve.

Natural Defense Mechanism

The human body, regardless of age or race, possesses an exceedingly effective defense mechanism against its first invasion with tubercle bacilli. Neutrophils and monocytes constitute the first two lines of defense. Lymphocytes enter the picture a little later. Lymphocytes normally predominate in the blood up to the age of four or five years. Thereafter, their percentage and absolute number gradually drops until the age of nine to 12 years, when the adult blood picture is established, which apparently persists for the remainder of life. For the ages of two to five years, the polymorphonuclear leukocytes constitute about 45 per cent and the lymphocytes 50 per cent. Between the ages of nine and 12 years, the polymorphonuclear leukocytes are 68 and the lymphocytes 29 per cent, which are the figures of adult life. Monocytes range from 3 to 6 per cent. No reference has been found to show that the ability of these cells to phagocytose organisms varies at different ages of life or in races of people. Irrespective of their portal of entry they are promptly phagocytosed by neutrophils, many of which enter blood and lymph streams. This is fortunate, for if all bacilli of the initial invasion remained at the site of entry, an exceedingly serious situation could obtain within a few months. Not all of the originally invading tubercle bacilli are ingested by a single neutrophil or are the numerous participating neutrophils focalized at the same point. If they were, a serious situation could soon obtain. Fortunately, the numerous tubercle-bacillus-bearing neutrophils circulating in the blood and lymph streams quickly lodge in various locations, so that relatively few organisms are deposited in one place. This is of tremendous advantage to the defense elements, including monocytes, lymphocytes, and fibroblasts in that they can cope more successfully with relatively few in each of many places than a large number in one location. Apparently, this accounts in part for the

almost uniform benignity of primary tuberculosis *per se*. The defense mechanism encountering relatively small numbers in any given place is able to surround them effectively before sensitivity to tuberculoprotein is well established and the subsequent more permanent encapsulation proceeds without interruption.

Obviously, if an overwhelming number of tubercle bacilli participate in the initial invasion, the defense elements may not be able to cope adequately at all of the points of focalization. Thus, when allergy appears, tuberculoprotein liberated from foci not well encapsulated may immediately produce reinfection type of tuberculosis. This was observed by Lemon and Montgomery[12] who introduced bovine type of tubercle bacilli into pleural spaces of healthy rabbits. Some of the bacilli remained in pleural spaces but others were phagocytosed and deposited in regional lymph nodes, and in remote organs. The immediate reaction was non-specific. The number of tubercle bacilli originally introduced was so large that many of the intracellular organisms could not be removed but remained within the lymph spaces or were included in cellular masses attached to the pleural surfaces. Up to this point, the reaction remained entirely non-specific. When the rabbit's tissues were demonstrably sensitized, the allergic tissues responded to reinfection as vast numbers of virulent bacilli were released. "The acute reactions and the lesions which bring about illness and death are final evidences of a specific reaction."

While with rare exception among people tubercle bacilli of first invasion are so well controlled by the defense mechanism as to cause only minute areas of destruction, the encased tubercle bacilli remain alive for indefinite periods of time. Sweany has shown that after foci of tubercle bacilli are well encased, even with calcium and bone, this material may be resorbed, thus liberating the organisms, resulting in endogenous reinfection. Implantations on allergic tissues are responsible for practically all of the acute and chronic destructive clinical tuberculosis. While the defense mechanism succeeds at least temporarily with many reinfections, it fails often enough to account for all the illness and death from tuberculosis among the people of the world.

Obviously, people possess a defense mechanism that protects far more effectively against the first invasion of tubercle bacilli than against subsequent attacks. The failures to protect against reinfections are the result of allergy to tuberculoprotein. This protein, released from tubercle bacilli of first invasion organisms, (before allergy appears) is innocuous. It offers no handicap to the defense mechanism. However, after allergy is established, tuberculoprotein becomes a violent poison to cells and tissues. Therefore, tubercle bacilli of reinfection require much more effort on the part of the defending elements and the response of these white blood cells is much greater in point of numbers than is true of primary infections. In fact, the response is so great that tubercle bacilli are temporarily held at their sites of invasion. This often results in serious destructive situations in that so many bacilli are present and so much tuberculoprotein is liberated in one place as to destroy the adjacent defending cells, as well as the

fixed tissues in the area. Thus, areas of necrosis of varying size are produced.

This temporary fixation of tubercle bacilli of reinfection at their sites of invasion was long misinterpreted as representing resistance thought to have been built up by the presence of tubercle bacilli in lesions of primary tuberculosis complexes. This erroneous concept resulted from conclusions drawn without sufficiently long periods of observation.[11]

The reaction is so intense and tuberculoprotein so poisonous that it is impossible for individual neutrophils to ingest and distribute bacilli to other places where, in small numbers, the defense mechanism would be more likely to succeed. Thus when large numbers of tubercle bacilli are suddenly discharged on allergic lung tissue, acute tuberculous pneumonia results and often so much necrotic material is expectorated that large pulmonary cavities are in evidence in a matter of weeks. When smaller numbers of tubercle bacilli invade allergic lung tissue, the defense mechanism may operate more successfully so as to reduce and hold the lesions in smouldering, chronic stages.

Anachronisms

Nearly a decade ago Wilson[12] employed the phrase "public health anachronisms" indicating "practices that are carried on now because they have been in use for the past thirty years or so even though it has been shown that they are of little or no value for the purpose for which they were originally intended." The field of tuberculosis now abounds with such anachronisms, including teachings and practices. The beliefs and teachings that people in certain ages of life, those of some races, and the mentally ill are more susceptible and have lower resistance to tubercle bacilli than others belong in this category as well as the belief that first infection type of tuberculosis protects against clinical disease.

SUMMARY AND CONCLUSIONS

Since 1920, longitudinal observations made on persons in various ages of life have revealed that: (a) Among 1,011 infants and young children infected, 30 (2.96 per cent) developed clinical tuberculosis. The others remained free from clinical disease during the period of childhood. (b) Among 2,979 children who reacted to tuberculin between the ages of 6 and 14 years, 137 (4.6 per cent) developed clinical lesions. (c) Chronic pulmonary tuberculosis usually made its debut during adolescence and throughout the remainder of life.

Among 2,266 persons who became infected at the age of 19 years or older and were recently traced, 2,080 with 24,431 person years of follow-up had developed no demonstrable tuberculous lesion. There were 54 in whom primary pulmonary infiltrates (Ghon tubercles in the inflammatory stage) cast visible x-ray shadows about the time allergy could be elicited. Pleurisy with effusion appeared in 67, mostly about the time allergy was detectable. Clinical reinfection type of tuberculosis subsequently developed in 65, of whom 60 had pulmonary and five extrathoracic lesions.

All demonstrable lesions behaved in the same manner as those previously observed in children and among adults who had been infected in childhood.

The natural defense mechanism of the human body apparently does not differ with age of life or races of people. Mental illness *per se* does not influence resistance.

The defense mechanism of the human body is handicapped when reinfections occur because of allergy which has been introduced following the primary invasion. Although the defense mechanism copes at least temporarily with many reinfections, it fails often enough to account for all the illness and death from tuberculosis.

RESUMEN Y CONCLUSIONES

Desde 1920 se ha hecho una observación a lo largo del tiempo en personas de edades diversas habiendo revelado tal estudio: (a) que entre 1,011 infantes y niños de corta edad infectados, 30 (2.96 por ciento) desarrollaron tuberculosis clínica. Los demás permanecieron libres de enfermedad clínica durante la infancia; (b) Entre 2.979 niños que reaccionaron a la tuberculina entre los 6 y 14 años de edad, 137 (4.6 por ciento) desarrollaron lesiones clínicamente comprobadas; (c) la tuberculosis pulmonar crónica generalmente hizo su principio durante la adolescencia y a través de todo el resto de la vida.

Entre 2,266 personas que se infectaron a la edad de 19 años o más y que fueron recientemente localizadas, 2,080 con 24,431 personas años de seguimiento, no han desarrollado lesión tuberculosa demostrable. En 54 personas de éstas, se observaron sombras correspondientes a infiltrados primarios (nodos de Ghon en estado inflamatorio) visibles a los rayos X cuando la alergia se descubrió. La pleuresía conderrame apareció en 67, la mayoría alrededor de la aparición de la alergia.

La tuberculosis de tipo reinfección se desarrolló subsecuentemente en 65, de los que 60 tenían lesiones pulmonares y 5 extrapulmonares.

Todas las lesiones demostrables evolucionaron del mismo modo que las antes observadas en niños y en adultos infectados durante la infancia.

Aparentemente el mecanismo natural de defensa en el cuerpo humano no difiere con la edad, las razas o las diferencias en los pueblos. Las enfermedades mentales por sí solas no influyen en la resistencia.

El mecanismo de defensa del cuerpo humano es desventajoso cuando ocurren reinfecciones con motivo de la alergia que se ha provocado des pués de la primoinfección. Aunque el mecanismo de defensa es eficaz por lo menos temporalmente ante muchas reinfecciones, bastante a menudo falla como para que permita la ocurrencia de todas las enfermedades y muertes por tuberculosis.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Seit 1920 an Personen verschiedener Lebensalter durchgeführte längsschnittmässige Beobachtungen haben ergeben, dass: (a) sich unter loll infizierten Kindern und jugendlichen Erwachsenen bei 30 (2,96%) eine klinische Tuberkulose entwickelte. Die anderen blieben frei von klinischer Erkrankung während der Periode der Kindheit; (b) unter 2979 Kindern,

die auf Tuberkulin reagierten im Alter zwischen 6 und 14 Jahren, entwickelte sich bei 137 (4,6%) klinisch manifeste Herde; (c) die chronische Lungentuberkulose nahm gewöhnlich ihren Anfang während der Jugendzeit und im Verlauf des späteren Lebens.

Aus einem Kreis von 2266 Personen, die sich mit 19 Jahren oder später infizierten und die jüngst nachkontrolliert wurden, hatten sich bei 2080 mit 24431 Personen-Jahren der Nachkontrolle keine nachweisbaren tuberkulösen Herde entwickelt. Es waren 54 Personen, bei denen primäre Lungeninfiltrate (Ghon'sche Tuberkel im entzündlichen Stadium) zu röntgenologisch sichtbaren Schatten führten ungefähr zu der Zeit, in der eine Allergie zustande gekommen sein konnte. Eine Pleuritis mit Erguss entwickelte sich anschliessend bei 67 Personen, meistenteils ungefähr zu dem Zeitpunkt, an dem eine Allergier feststellbar war. Formen mit klinischer Reinfektions-Tuberkulose entwickelten sich darauf folgend bei 65 Personen, von denen 60 pulmonale und 5 extrathorakale Herde hatten.

Alle nachweisbaren Herde verhielten sich in der gleichen Art und Weise wie diejenigen, die zuvor bei Kindern beobachtet worden waren und bei Erwachsenen, die in der indheit infiziert worden waren. Augenscheinlich ist der natürliche Abwehrmechanismus des menschlichen Körpers nicht verschieden in verschiedenen Lebensaltern oder Rassen oder Völkern. Geisteskrankheit als solche beeinflusst die Resistenz nicht.

Der Abwehrmechanismus des menschlichen Körpers ist gehandicapt, wenn Reinfektionen eintreten, infolge der Allergie, die sich im Anschluss an die erste Invasion entwickelt hat. Obwohl der Abwehrmechanismus mindestens temporär beeinflusst wird durch häufige Reinfektionen, sind ihm oft genug nicht alle Krankheits- und Todesfälle an Tuberkulose zur Last zu legen.

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The Acetylcholine Cough Test

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Pharmacological Applications in the Study of Anti-tussives
Pneumological Applications in the Determination of the Sensitivity of the Lungs

In man it is easy to initiate the cough reflex by inhalation of substances capable of exciting the sensory receptors of the lungs e.g. caustic substances (thymol, chlorine, ammonia,[1, 2] citric acid[3] or irritants such as dust and powders).

These products have the inconvenience, particularly as regards the caustic preparations, of being aggressive to protoplasms; their effect can be harmful at least in pathological subjects. Moreover the cough reaction produced may not be easily controllable and may be prolonged beyond the period desired.

A biological amine, acetylcholine, which we have observed, has the property of electively exciting the sensory nerve endings of the lungs[4, 5, 6] and of starting off the nervous impulses which induce coughing, does not have this inconvenience: it is neither caustic nor irritant.

The object of the acetylcholine cough test is to provoke a cough reaction by the inhalation of an aerosol of acetylcholine. The use of acetylcholine, as a cough stimulant, offers many advantages.

The acetylcholine cough test permits varying as desired the intensity of cough (by modifying the concentration of the dispersion) and its duration (by modifying the duration of the inhalation): it permits initiation and cessation of the cough reflex as desired and reproduction of the cycle at selected intervals.

The acetylcholine cough is readily controlled: interruption of the inhalation is sufficient to stop the cough usually fairly quickly; immediate cessation is obtained by inhalation of a hexamethonium aerosol.

The acetylcholine test is harmless and does not produce any general side-effects.

The acetylcholine cough test has two practical uses:

—applied in pharmacodynamics to determine the *effects of antitussive agents*

—in pneumology, it permits demonstrating at will *the normal excitability of the sensory nerve endings of the lungs* and provides a precise measurement of this pathological excitability

For the above reasons the acetylcholine cough test has a place among *the methods of exploration of pulmonary functions* and provides useful information in chronic pneumonopathies (asthma, emphysema, silicosis), in general and pulmonary surgery, in industrial medicine and in giving opinions in cases of respiratory affections.

Pharmacodynamic Considerations

The capacity of acetylcholine to excite the sensory pulmonary nerve endings, thereby releasing the cough impulse in the centripetal neurons, arises from a fairly general property of this substance, namely *its action on sensory nerve endings.*

Cough and excito-sensitive action of acetylcholine on sensory nerve endings

This property, still little known, represents a recent addition to pharmacology. From 1948 to 1954 several research workers showed that acetylcholine is capable of *exciting the sensory nerve endings.*

Brown and Gray[7] demonstrated that an injection of acetylcholine in the artery of a cutaneous region produces a discharge of impulses in the sensory nerve in that region.

In another sensitive region, the carotid gland, Douglas[8, 9] observed the stimulant action of acetylcholine and the inhibition of that action by hexamethonium.

More recently Douglas and Gray[10] showed that the sensory cutaneous excitant action of acetylcholine must be attributed to a direct action on the sensory tracts; hexamethonium inhibits this action but is not antagonistic to the sensitivity of the skin to touch which remains unchanged.

Finally Keele and his collaborators[11] indicated that acetylcholine applied on the exposed derma after excision of a cantharidal blister causes marked pain; a previous application of hexamethonium prevents the painful reaction but does not suppress the pain caused by contact.

The excito-sensitive action as well as the cough action of acetylcholine *are by no means physiological;* acetylcholine does not play any part in the sensory perception; neither does it have anything to do with the normal or pathological induction of the cough reflex.

The excito-sensitive action of acetylcholine and its action on cough are both *inhibited by methoniums* (penta and hexa) and this fact clearly emphasizes the relationship of these two actions.

The action on cough and the excito-ganglionic action of acetylcholine

The cough action of acetylcholine provokes *stimulation of a nerve cell* resulting in the release of a nerve impulse in the stimulated neuron. In consequence these actions are connected with a fundamental physiological action of acetylcholine: *the excito-ganglionic action.*

This action, termed nicotinic, is one of excitation, at the level of the ganglions, of the post-ganglionic neurons. Physiologically it ensures the passage of the nervous impulse of the preganglionic neuron (which liberates acetylcholine at its synaptic end) to the post-ganglionic neurons. This action is inhibited by the methoniums (penta and hexa). It is an elective antagonism related to the structural analogy (quaternary ammonium) of acetylcholine and the methoniums. It is admitted that this antagonism is the result of a so-called "competitive mechanism" between acetylcholine and the methoniums.

Fundamental differences separate these two actions.

—the excito-ganglionic action is *physiological*, whereas the cough action is not, but is purely *artificial*.

—the excito-ganglionic action is on the motor nerve tracts; the cough action is on the sensory nerve tracts.

On the other hand, these two actions are related on the following points:

—In both cases there is *excitation* of a *nerve cell* by acetylcholine. It is of interest to point out that the diversity of these two actions (cough and excito-ganglionic action) seems to imply that the neuronic excitant action may be a general property of the acetylcholine activity.

—In both cases this action is inhibited by the *same antagonists*: The methoniums (penta and hexa). This second phenomenon probably springs from the first.

Cough action of acetylcholine and its action on the motor effectors

This action, termed muscarinic, is on the smooth muscle and the glands. Physiologically it ensures the functional junction between the nerve and the effector which is the essential and final object of the cholinergic action. This action is inhibited electively by atropine.

These two actions are entirely dissimillar.

—The first is on a *nerve cell* whereas the second is on a motor effector, often a smooth muscle.

—The first is *artificial* but the second is *physiological*.

—Pharmacodynamic criteria show the fundamental differences of these two actions; specific antagonists demonstrate distinctly the differences (methonium for the cough action and atropine for the action on motor effectors).

On the other hand the two actions develop simultaneously (at least in cases of respiratory insufficiency) by administration of an acetylcholine aerosol.

—The excitation of the sensory nerve endings by acetylcholine produces a *cough reaction*

—The excitation of the pulmonary effectors causes a *ventilatory action* which is evidenced by diminution of vital capacity, maximum inspiratory volumes, and perhaps by transitory dyspnoea.

It should be noted that for the functional pulmonary study the two actions of acetylcholine, namely on cough and ventilation, provide complementary information:

—The cough action provides information on the *sensitivity* of the lungs.

—The ventilatory action gives information concerning their *dynamics*.

Technique

Three techniques can be used. The first, particularly simple, is the basic routine. The second, more precise, permits evaluation of the intensity of the cough reaction. The third, somewhat more delicate, measures the threshold of excitability of the pulmonary sensory receptors.

1.) Basic technique

The principle of the test is to give an inhalation of an acetylcholine aerosol and to observe if it causes coughing.

An aerosol is provided by the dispersion of 1 per cent aqueous solution of acetylcholine chloride. The duration of the inhalation is 90 seconds. If the cough reaction is too pronounced the inhalation is stopped. The object is simply to ascertain if the test is positive (production of a cough reaction) or not.

The simplicity of the test is apparent. No costly apparatus is required; only an aerosol generator is needed. The interpretation of the test presents no difficulty and its execution requires no technical specialist. The test is rapid and therefore causes no loss of time of personnel. It can be carried out at the bed-side and also because of its simplicity, speed and economy, it can be used for the simultaneous examination of a large number of patients.

The test is harmless. Coughing ceases soon after discontinuing the inhalation. If necessary, administration of a hexamethonium aerosol will stop the cough immediately.

The only disadvantage, which is insignificant, of the test is that in the asthmatic patient there is a risk of a dyspneic reaction. This is always readily reversible and in any case can be immediately checked by atropine or adrenergic substances; for example, inhalation for one or two minutes of an atropine aerosol (dispersion of a 0.04 per cent aqueous solution of atropine sulfate) or of isoprenaline (dispersion of a 0.2 per cent aqueous solution).

2.) Technique for the graphic recording of the cough reaction

For a more precise study it is preferable to record by graphs the cough reaction produced. The assistant in charge of the patient receiving the inhalation of acetylcholine aerosol sets in motion an electro-magnet which records the phases of the cough on the cylinder rotating at 0.5 cm. per

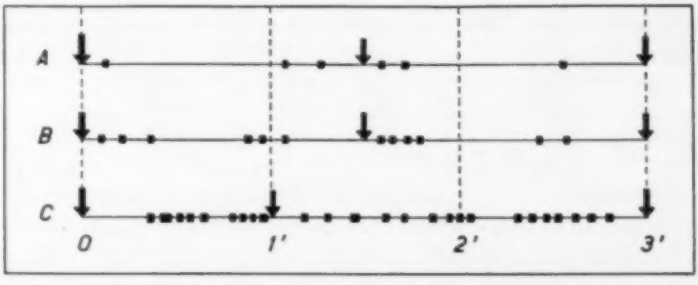

FIGURE 1: Recording of cough reaction provoked by acetylcholine—The three cough reactions are: (A) slight, (B) moderate and (C) marked. (From *LePoumon et le Coeur*, 11:385, 1955.)

The first and second arrows of each figure indicate the onset and termination of the inhalation; the third arrow indicates the termination of the recording.

The vertical lines show the time in minutes from the beginning of the test.

Concentration of the acetylcholine dispersion inhaled: 100 μg per liter.

second. The frequency and duration of the periods of coughing are thus recorded. Figure 1 shows graphs of three different cough reactions, slight, moderate, and pronounced.

As in the basic technique, inhalation of a dispersion of a 1 per cent aqueous solution of acetylcholine is applied for 90 seconds. The recording of the cough is continued for 90 seconds following the inhalation. If the cough reaction is so pronounced as to necessitate interruption of the inhalation, in order to control the cough over a sufficiently long time it is preferable to use a less concentrated aerosol by dispersing a more dilute solution of acetylcholine e.g. 0.5 per cent to 0.3 per cent or even 0.1 per cent.

The graphic recording has the advantage of giving greater precision to the acetylcholine cough test and the results furnish more satisfactory details on the character of the cough. It also permits the ascertainment of the number of attacks of cough induced by the inhalation of acetylcholine as well as giving information on the overall duration of the cough (total duration of each attack of coughing).

The comparison of these results with those obtained later gives a clear picture of the modifications which the excitability of pulmonary sensory nerve endings can undergo.

Still more precise is the measurement of the threshold of excitability.

3.) Measurement of the threshold of excitability

This technique involves the finding of the weakest concentration of the dispersion of acetylcholine capable of starting the cough reflex.

With this object in view an aerosol is applied every five to 10 minutes for 15 seconds; at each application the concentration is increased.

The aerosols are produced in a generator under compressed air of 800 g. per cm. 2; the liquid volume of the generator is 0.2 ml. per minute and its vapor volume is 20 liters per minute. Under these conditions a 1 per cent solution of acetylcholine is dispersed and one liter of aerosol contains 100 μg of acetylcholine.

The following are the various concentrations of acetylcholine solution we use successively:

0.1	per 100
0.25	per 100
0.5	per 100
1	per 100
2.5	per 100
5	per 100

These progressively increasing concentrations providing increases of 200 per cent to 250 per cent at each application will furnish sufficiently precise data. It will be seen that the highest concentration is 50 times greater than the weakest thus giving a sufficient margin to allow for common pathological alterations of the excitability of the pulmonary sensitive nerve endings.

With these successive tests, it is possible to ascertain the weakest concentration capable of provoking cough. It can be termed the "threshold concentration" and may be verified by two additional tests. For example, a test with a weaker concentration should not produce coughing and would therefore confirm that it is a "sub-threshold concentration." A larger concentration than the threshold dose should produce more pronounced coughing, thereby evidently confirming that it is a "supra-threshold concentration."

Ascertaining the threshold of excitability is generally simple but sometimes it can be a little awkward. For example, the attacks of cough during the first seconds of the inhalation can give rise to errors: it may happen that they are not reproduced even with higher concentrations of acetylcholine. Also some minor coughing spasms may be a chance occurrence. In these circumstances the test would only permit ascertaining the threshold of excitability if a further inhalation reproduced them and if an inhalation of a greater concentration produced a more marked cough reaction.

Characteristics Of The Cough Produced By Acetylcholine

I. Frequency of the acetylcholine cough

Of the patients seen by us for affections of the respiratory tract (chronic bronchitis, emphysema, asthma, fibrous tuberculosis, pulmonary sclerosis) in winter 80 to 90 out of 100 react to the acetylcholine cough test (aerosol containing 100 μg per liter), but in summer the proportion is considerably less.

The acetylcholine cough test is also frequently positive in patients with transitory inflammatory conditions of the respiratory tract (winter colds). It is sometimes positive in normal people provided aerosols based on stronger concentrations are used (500 μg per liter).

II. Intensity of the acetylcholine cough

The intensity of the acetylcholine cough varies. Sometimes it is slight; one or two brief coughing spasms interrupting the inhalation. Sometimes however the cough is intense either as regards to frequency (almost continued coughing) or violence. In the violent reactions the coughs are accompanied by congestion of the face and exceptionally by a slight but transitory faintness or black-out reminiscent of a tussive syncope.

The cough reaction can be manifested by isolated spasms of cough or a series of cough spasms more or less prolonged separated by intervals of varying lengths.

When the cough is slight it can be voluntarily and entirely suppressed or suppressed for a short time. However, when the cough is more pronounced it is no longer controllable. Although the attacks can be delayed voluntarily for some seconds, when they are so delayed the ensuing cough spasms are usually more violent and more prolonged than if the patient had not tried to prevent their onset.

These observations show that in a comparative study of the cough reactions to acetylcholine, errors can arise in the interpretation of slight coughs which can be modified voluntarily. Errors of interpretation are not likely

to occur when the cough reactions are pronounced where the voluntary control mechanisms are insufficient to modify the cough reflex to a marked degree.

III. Rapidity of onset of the cough in the acetylcholine test

With the acetylcholine test the onset of cough is rapid and appears often during the first inspirations of the aerosol. In some instances, there may be a delay of 30 to 60 seconds and in a few cases the cough may not even appear during the inhalation but only after it has been discontinued.

Sometimes the cough reaction is in two successive phases. In the first phase the cough spasms appear at the beginning of the inhalation and last only from five to 10 seconds. In the second phase, separated from the first by an interval of from 15 to 30 seconds, the coughing periods are more prolonged and continue up to the termination of the inhalation and sometimes beyond it.

IV. Duration of acetylcholine cough

The cough reaction persists during all the period of inhalation but ceases on its termination. Frequently the cessation of coughing is immediate but sometimes coughing continues for about a minute after stopping the inhalation. This is the reason we continue recording the cough for 90 seconds after stopping the inhalation. Rarely does the patient continue coughing after discontinuing the recording.

The rapidity of cessation of cough after interruption of the inhalation shows to what extent the acetylcholine cough is controllable. This property emphasizes the harmlessness of the test and its convenience in general practice.

The rapidity of cessation of the cough reaction is characteristic of the

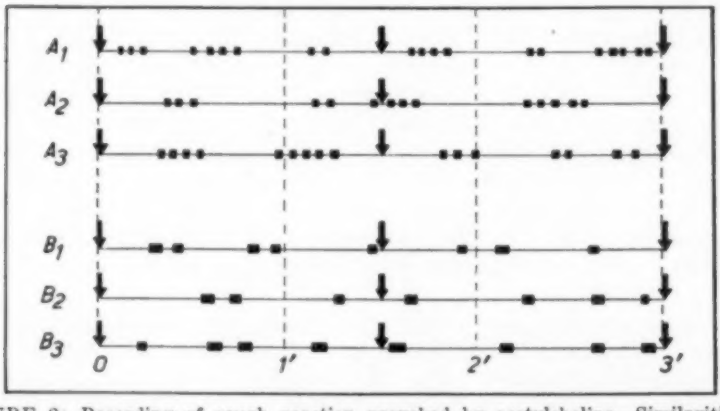

FIGURE 2: Recording of cough reaction provoked by acetylcholine—Similarities of cough reactions in successive experiments. Two examples. (From *LePoumon et le Coeur*, 11:385, 1955.)

See Legend under Figure 1.

A_1, A_2, A_3. Three recordings each at 15 minute intervals of the acetylcholine cough provoked on the same patient. It is seen that the three cough reactions are strictly similar.

B_1, B_2, B_3. As above, experiment on a different patient. Same observations as above.

action of acetylcholine. All acetylcholine effects seen in experimental pharmacology (effects on heart, tension, intestines) are almost immediately reversible; it is known that this is due to the instability of acetylcholine which is rapidly destroyed by cholinesterase.

V. Relation of the cough to the method of administration of acetylcholine

The intensity of the cough reaction is closely related to the concentration of the acetylcholine inhalation but is not influenced by the duration of the inhalations or their repetition.

1.) Concentration of the dispersion

The higher the concentration of the acetylcholine dispersion the more pronounced is the cough reaction (see above: Measurement of the threshold of excitability).

2.) Duration of inhalation

The intensity of the cough reaction is not influenced by the duration of inhalation.

If inhalation is continued for three minutes, the cough produced has the same characteristics (intensity, frequency, and duration of the spasms of cough) during the third as during the first minute. Cough reaction is not intensified by prolonging the inhalation.

3.) Repetition of inhalations.

If several aerosol inhalations are applied successfully at 15 minute intervals for example, the aerosol cough reactions are of the same type.

They are not absolutely identical when the cough reaction is slight. This is not surprising seeing that cough is a complex phenomenon influenced by numerous neuronic factors in which not only the usual centers (cough center) participate but also influences from the cerebral cortex which can markedly influence the intensity of the cough response. Despite these variations which can result from the various influences, the acetylcholine cough reaction is shown by successive tests to remain fairly constant (see Figure 2).

Although there may be some differences between one recording and another the graphs obtained from successive inhalations with acetylcholine show striking similarities. Both the number of cough spasms and the overall duration of the cough (total of the duration of each cough spasm) show only moderate variations in a given series of tests.

This factor is of interest in applied pharmacology as it permits using the criteria for the comparative study of cough sedatives (see Fig. 3).

VI. Symptoms accompanying the acetylcholine cough

Different subjective sensations often accompany the cough. They are described by patients in various ways:

—Slight sensation of tickling; feeling of a feather moving in the respiratory passages

—More pronounced tickling provoking itching

—Prickling or tickling sensation

—A feeling of prickling or more or less pronounced pricks as is caused by the presence of needle points

—A feeling of local warmth or even burning

—Sometimes a feeling that there is an obstruction of the respiratory tubes stopping the passage of air; in these cases the resultant cough seems to be due more to a voluntary act to expel the cause of obstruction than to a dominant reflex.

These sensations are usually felt in a fairly restricted zone. Zones most often concerned are the pharyngo-laryngeal and the retro-sternal. Sometimes the sensations are in restricted areas and can be described as lenticular or punctiform.

The sensations increase progressively during the acetylcholine inhalation; the cough occurs when they have reached a certain intensity and coughing causes them to disappear momentarily. Sometimes they are superseded, after the cough, by a feeling of burning.

These subjective sensations are less acute or even disappear completely when the acetylcholine inhalation is accompanied or preceded by the inhalation of an aerosol of penta or hexamethonium which is able to suppress the acetylcholine cough. When cough is inhibited by these antagonists the subjective sensation can persist although in a milder form.

This confirms that the cortical centers of perception are more sensitive than the cough centers; a weak stimulation can produce a subjective sensa-

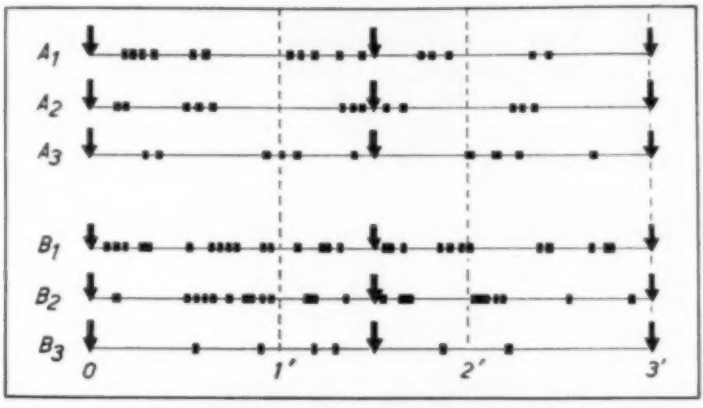

FIGURE 3: Recording of cough reaction provoked by acetylcholine—Effect of antagonists to the acetylcholine cough: (A) Codeine and (B) L.1633.* (From *Le Poumon et le Cœur*, 11:385, 1955.)

See Legend under Figure 1.

Concentration of the acetylcholine dispersion; 100 μg per liter.

A—Codeine = A_1: first test.
A_2: second test, 30 minutes after the preceding test.
A_3: third test, 30 minutes after administration of 0.04 g codeine.
— Inhibitory action on the cough.

B—L.1633* = B_1: first test.
B_2: second test, 30 minutes after the first.
B_3: third test, 30 minutes after administration by mouth of 0.06 g of L.1633.*
— Definite inhibitory effect on the cough.
Experiment carried out on an asthmatic patient.

*di-terbutyl naphthalene sulfonate sodique.

tion but insufficient to release the cough reflex which requires a more pronounced stimulation.

VII. Inhibition of the acetylcholine cough by certain antagonists

These antagonists can be divided into three groups:

1.) Inhibitors of the cough center

This group includes morphine and its methyl (codeine) and ethyl (codethyline) derivatives.

The inhibitory action on cough of these products is moderate, inconstant and always incomplete. It is not manifested when the cough reaction is pronounced but only in cases of mild cough.

The inhibitory action on the cough of morphine and its derivatives is not the result, even partly, of a local pulmonary effect on the pulmonary sensitive receptors; a codeine aerosol (dispersion of a 2 per cent aqueous solution of codeine phosphate), given during five minutes before the acetylcholine inhalation does not in the least modify the cough reaction of acetylcholine. The action of morphine and its derivatives seems therefore to be exclusively central.

2.) The eupneics

These include atropine, adrenergics and to a lesser degree the xanthines.

Their inhibitory action on cough is more particularly apparent in cases of respiratory insufficiency. This action is definite; it sometimes leads to a complete suppression of cough but more often to a marked diminution.

The eupneices are not direct antagonists to the excitant action of acetylcholine on the pulmonary sensitive nerve endings. They seem to act on the sensitive mechanism in diminishing their excitability (see below: Mechanism of the cough action of acetylcholine).

3.) The elective antagonists of acetylcholine cough

This group includes sparteine, penta and hexamethonium and a derivative of khelline,* amikhelline.

Moreover, all these products possess ganglioplegic properties** which are antagonistic to another action of ectylcholine, namely the excito- ganglionic action, termed nicotinic action.

The intensity of the inhibitory action on the cough varies according to the drug used in this group; it is weak with sparteine, well defined with amikhelline, and marked with penta and especially hexamethonium. The two latter substances suppress almost always completely the most intense cough reaction produced by acetylcholine (See Fig. 4). To obtain an inhibitory action on cough by these substances it is useless to inject them; it is sufficient to give them in the form of an aerosol† by which means the general and unde-

*We have not been able to ascertain whether khelline also exercises this action. Its solutions are too irritant to administer them via the respiratory tract.

**It has not been definitely established that amikhelline possesses these properties.

†The concentrations of the aerosol solutions used are:
—Sparteine. Sparteine sulfate 2:100.
—Amikhelline. Amikhelline hydrochloride 2.5:100 (Nokhel Houdé).
—Penta methonium. Dibromide of pentamethyl-pentylene diammonium 5:100 (Pendiomide Ciba).
—Hexamethonium. Dibromide of hexamethonium 1.15:100 (Hexanium Adrian).

sired effects of these products (hypotension in the case of the methoniums) are avoided.

The effect of these products is immediate. In a person who reacts with intense attacks of coughing to inhalations of acetylcholine, the administration of an aerosol containing acetylcholine and hexamethonium (dispersion of a solution containing 1:100 acetylcholine and 1.15:100 of hexamethonium dibromide) does not produce any cough reaction (see Figure 4).

These substances exercise a direct anti-acetylcholine action; they inhibit electively the excitant of acetylcholine on pulmonary sensitive nerve endings.

Mechanism Of The Cough Provoking Action Of Acetylcholine

To study this mechanism the following were investigated:

—the site of the cough action of acetylcholine

—the mode of action of acetylcholine

A) Site of the Cough Provoking Action of Acetylcholine

All considerations suggest that acetylcholine stimulates the cough reflex arc at the place of its origin, namely pulmonary sensory nerve endings.

This hypothesis is confirmed by the following:

1.) Acetylcholine does not have an extrapulmonary action

The cough produced by inhalation of acetylcholine is often immediate; a single inspiration of from 300 to 500 ml. of an acetylcholine aerosol containing 100 μg of acetylcholine per liter is sufficient to start coughing spasms immediately. Despite the rapid absorption in the general circulation of the substances administered in the form of aerosols, the inhalation of a dispersion of acetylcholine would not be able to produce such an *instantaneous* effect if its site of action was extrapulmonary.

Moreover the quantity of acetylcholine inhaled during a single inspiration (from 30 to 50 μg) of an acetylcholine aerosol is too weak to permit the substance passing into the blood in a sufficient concentration to be active.

It has been established that when acetylcholine is introduced into the organism by means of an aerosol it has no extrapulmonary destination. It is destroyed by the action of cholinesterase as soon as it is absorbed into the alveolar capillaries.

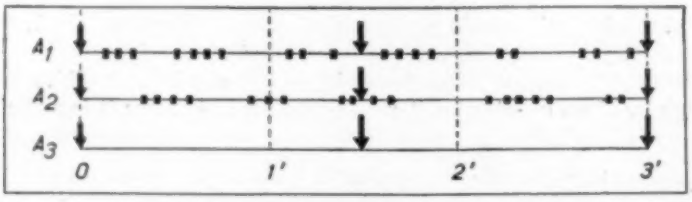

FIGURE 4: Recording of cough reaction provoked by acetylcholine—Anti-acetylcholine action of hexamethonium. (From *Le Poumon et Le Coeur*, 11:385, 1955.)
See Legend under Figure 1.
A_1: Inhalation of a dispersion containing 100 μg of acetylcholine per liter.
A_2: Ditto, 30 minutes later. Cough reaction similar to that in the preceding test.
A_3: Inhalation of a dispersion containing 100 μg per liter of acetylcholine and 115 μg of hexamethonium dibromide per liter.

In dogs the inhalation of an acetylcholine aerosol does not have any general action (cardiovascular effect, for example) but such an action occurs (hypotension) if the animal receives physostigmine (inhibition of cholinesterase).[12]

2.) Acetylcholine stimulates the pulmonary sensory nerve endings

Acetylcholine being unable to exercise any extrapulmonary action when administered by aerosol, the release of the cough reflex can only arise via stimulation of the sensory nerve endings of the pulmonary epithelium.

This stimulation is manifest by the diverse subjective laryngo-tracheo-bronchial sensations of tickling and prickling felt by the patient during the inhalation of the acetylcholine aerosol.

B. Mechanism of Action of Acetylcholine

The fact that inhalation of an acetylcholine aerosol provokes excitation of the cough reflex via the pulmonary sensory nerve endings does not absolutely imply that such excitation results from a *direct action* of acetylcholine on these nerves.

This excitation could be the result of *an indirect mechanical action* (compression, distension) as a consequence of the ventilatory motor effects of acetylcholine. It could also be the result of *an indirect chemical action* brough about by a medium such as histamine.

1.) Direct action

Several factors support this hypothesis.

It should be first recalled that contrary to the ventilatory effect, the cough reaction *ceases immediately* or shortly after stopping inhalation of acetylcholine. If the cough was the result of a mechanical influence due to the ventilatory effect of acetylcholine it would be much more prolonged and *would persist as long as the latter effect*, that is frequently for from 15 to 30 minutes after the end of the inhalation.

On the other hand, the acetylcholine cough can, at least in certain cases, be produced despite a previous administration of atropine or an adrenergic, which inhibits completely the appearance of the ventilatory effects of acetylcholine. In these cases the cough stimulus via the pulmonary sensitive nerve endings is evidently not due to mechanical irritation caused by the ventilatory effects of acetylcholine.

Moreover, prior administration of antihistamine aerosols does not inhibit or diminish the cough reaction provoked by acetylcholine. It does not seem therefore that the acetylcholine cough results from an indirect chemical excitation of the cough sensitive receptors by histamine.

Finally a predominant argument in favor of the direct excitation of the sensory nerve endings by acetylcholine is supplied by the fact that the penta and hexamethoniums suppress to a remarkable degree, and frequently completely, the cough reaction produced by acetylcholine aerosols.

It has been shown above (see under "Pharmacological considerations") that penta and hexamethoniums have varied properties; they antagonize electively the excitant effects which acetylcholine exercises on the nerve cells—excito-ganglionic and excito-sensitive action. Seeing that the methon-

iums antagonize the acetylcholine cough, it is logical to admit that the cough produced by acetylcholine is the result of this substance having a direct excitant effect on the sensitive nerve endings.

It could not be through combating a possible irritant action of a mechanical nature resulting from the ventilatory effects of acetylcholine that penta and hexamethoniums suppress the acetylcholine cough because these substances do not exert any antagonistic action on the ventilatory effects of acetylcholine. Thus the administration of an aerosol of penta or hexamethonium *suppresses only the cough provoking effects of* acetylcholine and *not its ventilatory effects.*

These various factors suggest that the acetylcholine cough is the result of a direct stimulation by acetylcholine of the sensitive nerve endings of the pulmonary epithelium.

2.) Indirect action

Other findings show that acetylcholine also exhibits an indirect action on cough by the intermediary of its ventilatory effects (the so-called muscarinic action of acetylcholine on pulmonary effectors; smooth muscles, glands).

If prior to applying the acetylcholine aerosol, an inhalation of an atropine aerosol consisting of a dispersion of a 0.04:100 aqueous solution of atropine sulfate is given for from two to five minutes (atropine by aerosol inhibits completely the production of the ventilatory effects of acetylcholine) the acetylcholine cough reaction is markedly diminished and sometimes suppressed.

a.) Of course it can be asked if the atropine is not capable of antagonizing the excitant action of acetylcholine on the sensitive nerve endings.

This question warrants examination because of the two following factors:

(1) As we have just seen, the action of acetylcholine on the sensory nerve endings would be of the same type as its excito-ganglionic action.

(2) On the other hand it seems that in certain experimental conditions (strong doses), atropine, besides its anti-acetylcholine action on the motor effector nerves (inhibition of the muscarinic action of aectylcholine) can exert an anti-acetylcholine action on the ganglions (inhibition of the nicotinic action of acetylcholine).

It is seen that the relationship of these two factors is a justification for the hypothesis of an inhibitory action of atropine against the excito-sensitive cough action of acetylcholine.

b.) Whatever the justification for this hypothesis, it is certain that atropine diminishes the acetylcholine cough by inhibiting the ventilatory effects of acetylcholine. Moreover, all substances capable of opposing the ventilatory effects of acetylcholine diminish, like atropine, the cough reaction.

This is particularly the case for adrenergics; isoprenaline (0.2:100) dioxyephedrine (1:100) when they are administered in the form of aerosols before the inhalation of acetylcholine.

c.) The mechanism by which the ventilatory motor action of acetylcholine contributes to the cough provoking effect of acetylcholine is worth studying.

It does not seem that the ventilatory motor action of acetylcholine (except when it is intense) should be sufficient to provoke cough.

If this were the case the cough reflex would continue to be maintained as long as the ventilatory effect produced by acetylcholine lasts (sometimes from 15 to 45 minutes); that however is not the case as the cough stops almost immediately after cessation of the inhalation of the acetylcholine aerosol.

Moreover, if the motor ventilatory action of acetylcholine alone was sufficient to provoke cough, the latter would not be suppressed by the methoniums in as much as they do not all modify the ventilatory effects of acetylcholine.

These considerations have induced us to admit that the ventilatory motor action of acetylcholine would result in *increasing the excitability of the sensory nerve endings*, but would be *insufficient to induce the cough reflex; this latter process would result only from the direct excitant action of acetylcholine on the sensory nerve endings.*

However, for acetylcholine to provoke a cough reaction, it is necessary that the excitability of the sensory nerve endings should be pathologically increased.

3.) Pathological excitability of the sensory nerve endings

We still know only imperfectly the cause of this pathological excitability. Nevertheless, it has been possible to make the following observations:

a.) The acetylcholine cough reaction is always marked when there exists *a condition of pulmonary irritation.* This condition, which is characteristic of pulmonary emphysema, is manifested by a non-specific abnormal sensitivity to all hexogenic irritants (certain sharp odors in kitchen fumes, cigarette smoke) which provoke cough and aggravate dyspnoea.

b.) The acetylcholine cough reaction is also a consequence of *inflammatory conditions of the respiratory apparatus.* It is seen in cases of acute and chronic bronchitis, pulmonary suppuration, and generally when there is purulent expectoration.

c.) However, the acetylcholine cough can be observed independent of these pathological processes in persons who are not sclero-emphysematous and in those who have no inflammatory conditions of the lungs; the hyperexcitability of the sensitive nerve endings seems therefore to be primary. Examples of these possibilities are found in patients with spasmodic tracheitis and certain asthmatics.

In these instances the acetylcholine cough seems to result from a pathological process affecting electively the sensory neurons of which the endings become abnormally sensitive.

These observations suggest that three factors intervene in the mechanism of the acetylcholine cough.

1.) A *pathological excitability* of the sensory nerve endings.

This factor is indispensable for the production of the cough reaction: acetylcholine does not cause cough in normal people unless aerosols of high concentration (500 μg or more of acetylcholine per liter) are used.

2.) An *increase* of this *excitability* by the ventilatory motor action of acetylcholine.

This action is suppressed by atropine. This second factor is facultative; it augments the acetylcholine cough.

3.) A direct *excitant action* on the sensitive nerve endings by acetylcholine.

This action is suppresed by penta and hexamethoniums. The latter factor alone permits the release of the cough reflex.

Practical Application

The cough provoked by the acetylcholine test is of practical value in pharmacology and pneumology.

Applications in pharmacology

In this field it provides a means of verifying the activity of antitussives. Two methods can be followed. The first consists of comparing the cough reactions registered before and after administration of the anti-tussive, for which comparison the overall duration of the cough reaction is taken into account, i.e., the total of the duration of each cough spasm—see Fig. 3 concerning tests with codeine and L.1633.*

The second concerns the comparison of the threshold of the cough excitability of the lung before and after administration of the substance studied.

This threshold is measured and expressed by the weakest concentration (threshold concentration) of acetylcholine aerosol inhaled capable of provoking a definite cough reaction.

Under the influence of the anti-tussive, an increase, more or less pronounced of the threshold of excitability is observed (increase of the threshold concentration) which characterizes the intensity of the inhibitory effect on cough.

Applications in pneumology—Asthma

The acetylcholine cough test is of no interest in the diagnosis of asthma. In asthmatics with pronounced cough a positive reaction to the cough test is frequently due to an infectious tracheo-bronchial catarrh; but if positive reaction is independent of any infection it suggests the presence of a primary hyper-excitability of the sensitive nerve endings similarly as in spasmodic tracheitis.

This possibility is fairly frequent in cases of asthma when there is increased acetylcholine excitability on the one hand, of the pulmonary motor effectors (smooth muscles etc.) from where the ventilatory effect of acetylcholine arises, and, on the other hand, of the sensory nerve endings from where the cough provoking effect of acetylcholine originates. This hyper-excitability concerning at the same time the motor and sensitive nerves seems to be the origin of the two clinical symptoms presented by these patients, namely the dyspnoea and the cough.

*di-terbutyl naphthalene sulfonate sodique.

Chronic respiratory insufficiencies

A cough reaction can be the fleeting expression of a transitory inflammatory condition, for example onset of bronchitis in winter.

However, if the acetylcholine cough occurs independent of any inflammatory process and particularly if it is repeated on making successive examinations at intervals of one or two months, it can generally be interpreted as being due to an irritative condition of the pulmonary epithelium resulting in an increased sensitivity to all exogenous irritants such as kitchen and tobacco fumes. This irritative condition does not signify a favorable prognosis: it always accompanies pulmonary emphysema of which it is one of the most constant symptoms. The development of emphysema constitutes the most troublesome lesion in respiratory insufficiency.

Industrial medicine—Detection of workers whose activities might have ill effects on their lungs

In certain industries workers are in polluted atmosphere (presence of gases or caustic chemicals) which can be injurious to those whose respiratory apparatus is somewhat weak. Radiography is not capable of detecting such cases but the acetylcholine cough test seems to be of value in this respect. In detecting the hyper-excitability of the pulmonary sensory nerve endings, it seems that it provides a method permitting the revelation of very diverse pathological processes which combine to cause an increase of the excitability of the sensitive receptors of the lungs.

In this connection, only trials on a sufficiently extensive scale would permit the confirmation of the value of the acetylcholine test.

It would also be highly interesting to know if the acetylcholine cough test would be capable of identifying people most susceptible to the risk of silicosis.

In the mines of Sarre (Claass—personal communication) it has been observed that miners with silicosis respond strongly to the acetylcholine cough reaction; we have made similar observations in a small series of 20 patients.

General surgery

It is not without interest for surgeons and anesthetists to know the conditions of patient's lungs prior to operation and in particular to be informed of patients whose respiratory apparatus is abnormally weak.

Information of this type is ascertained by means of the acetylcholine cough test. This convenient, quick and economical test, which is easily made even at the bedside, ought to be carried out systematically not only prior to all important surgical interventions but also on aged persons suspected of having pulmonary troubles—bronchitic patients, those who have had in the past some lung trouble.

The confirmation of an acetylcholine cough reaction can be a guide to subsequent treatments:

—it would always indicate a treatment by aerosols of antibotics before and after operation

—it can sometimes indicate the advisability of postponing the day of the operation or suggest modifications of the intended technique

—it can also provide guidance as to the choice of the anesthetic substance to be used.

Pulmonary surgery

Information on the function of the patient's lungs is one of the factors in which are based the indications for pulmonary surgery.

Results of the acetylcholine cough test have a place among the details obtained from the general examination to gain knowledge of the patient's lungs

A definitely positive cough reaction must always be interpreted as an aggravating factor. It indicates the risk of the development of infection or emphysematous conditions.

Appraisal of respiratory infections

To establish the disease rate caused by pulmonary infections of a dyspneic character, the investigator has to base his opinion, in part, on the findings obtained from the examination of the patient's lungs. It would be useful to incorporate in those findings the reactions of the patient to the acetylcholine test.

A definite cough reaction to the acetylcholine test in a patient whose ventilatory function is markedly disturbed is a certain aggravating factor indicating, as we have seen, emphysema or infection.

It could be asserted that cough is easily simulated. But, because of the antagonistic action of hexamethonium which suppresses the cough reaction provoked by acetylcholine, it is not difficult to detect malingerers.

Pharmacological considerations

The cough provoking action of acetylcholine presents various characteristics in common with other actions of acetylcholine.

—It constitutes one aspect of a more general action of acetylcholine, namely the *excito-sensitive* action of acetylcholine.

—The cough provoking action presents close functional similarities with the *excito-ganglionic action*, the so-called nicotinic action of acetylcholine; in both cases the action is on nerve cells.

—On the other hand cough provoking action of acetylcholine is fundamentally different from the *action* of acetylcholine on the *pulmonary effectors* (smooth muscles, glands) of the autonomic nervous system which is responsible for the ventilatory effect of acetylcholine. Both these two actions, namely cough provoking and ventilatory are produced simultaneously by the administration of an aerosol of acetylcholine; they can be pharmacologically dissociated; they provide complementary factors permitting the study of the sensitivity and motility of the lungs.

Technique

Three techniques are used.

The first, particularly simple, is for routine use.

The second, more precise, permits the evaluation of the intensity of the cough reaction.

The third, a little more delicate, measures the threshold of excitability of the pulmonary sensory receptors.

Characteristics of cough

Cough appears quickly after beginning of inhalation but ceases as soon as it is interrupted; therefore it is easily controlled. This property demonstrates the harmless character of the acetylcholine cough test and makes obvious its avantages for use in general practice.

Intensity of the cough is determined by concentration of acetylcholine solution used for the aerosol but is not influenced by the duration of the inhalation or by its repetition.

Mechanism

Various findings show that acetylcholine cough results from direct excitation by acetylcholine of the pulmonary sensory nerve endings. The predominant finding is supplied by the fact that the methoniums (penta and hexa) which are inhibitors of the effect of acetylcholine on nerve cells suppress the acetylcholine cough.

Practical application

The acetylcholine cough test is of practical value in parmacology for the study of anti-tussives in pneumology where it permits measurement of the pathological excitability of the pulmonary sensory nerve endings; in this connection it can provide useful diagnostic and prognostic information in cases of asthma and in cases of chronic respiratory insufficiency. The test is also of value in industrial medicine, in general and pulmonary surgery and in obtaining statistics of respiratory affections.

SUMMARY

Acetylcholine administered in the form of aerosol is an excitant of the sensory nerve endings of the lung. It provokes cough impulses when these sensitive mechanisms are abnormally excitable. The acetylcholine cough test registers this pathological excitability of the pulmonary sensory nerve endings.

RESUMEN

La acetilcolina administrada en aerosol es un excitante de las terminales sensoriales del pulmón. Provoca impulsos de tos cuando estos mecanismos son anormalente excitables. La prueba de la tos provocada por la acetilcolina, denuncia esta excitabilidad de las terminales nerviosas pulmonares.

RESUME

L'acétylcholine administrée sous forme d'aérosol est un excitant des terminaisons nerveuses du poumon. Elle provoque des crises de toux lorsque ces dispositifs sensitifs sont anormalement excitables. Le test de la toux à l'acétylcholine enregistre l'excitabilité pathologique des terminaisons des nerfs sensitifs du poumon.

ZUSAMMENFASSUNG

Acetylcholin in der Verwendungsform des Aerosols ist ein Reizmittel für die sensorischen Nervenendigungen der Lunge. Es ruft Hustenreiz hervor, falls diese sensiblen Mechanismen abnorm erregbar sind. Der Acetylcholin-Husten-Test registriert diese pathologische Erregbarkeit der pulmonalen sensorischen Nervendigungen.

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Pulmonary Stenosis with Left-to-Right Shunt: A Physiological Variant of Fallot's Tetralogy*

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One combination of cardiac anomalies not previously recognized but now encountered with increasing frequency is that of pulmonary stenosis, ventricular septal defect, and preponderant left-to-right shunt through the ventricular septal defect. This has been recognized in both the pure form and in combination with other cardiac deformities. Eight adult patients ranging in age from 17 to 53 years have been studied who presented with this combination. In only one instance was cyanosis present at rest.

Methods

In addition to the history and physical examination, electrocardiograms and cardiac fluoroscopy were done. In each instance, cardiac catheterization was carried out by the usual techniques and blood gas analyses were done using the method of VanSlyke and Neill. Pressures were recorded through the cardiac catheter with a strain gauge transducer and a direct writing recording instrument. Cardiac output and the left-to-right shunt in each instance were determined by the application of the direct Fick principle. The results of the catheterization studies are given in Table I.

Clinical Findings

In each instance, the presenting complaint was dyspnea on effort with the exception of one patient who had no symptom whatsoever. No patient in the group was thought to be more severely disabled than a functional class II. All of them were either gainfully employed or were students. One, age 53, was cyanotic at rest. Four had noted cyanosis of a mild degree on

TABLE I

Case	Pressures, mm. Hg.			Oxygen Sat. %				Flow, liter/min.		
	P.A. (mean)	R.V.	R.A. (mean)	P.A.	R.V.	R.A.	Fem. A.	Pulm.	Syst.	Shunt
1.	10	79/7	8	80	72	68	95	4.4	2.61	1.8
2.	8	86/2	3	76	78	65	94	4.3	2.7	1.6
3.	12	138/6	5	78	69	69	93	5.0	3.1	1.9
4.	9	80/8	4	76	73	64	91	6.2	3.5	2.7
5.	13	92/8	6	88	82	77	97	10.6	5.3	5.3
6.	17	70/5	5	90	90	77	98	....	....	....
7.	17	79/6	4	91	79	78	99	11.9	5.0	6.9
8.	7	84/3	4	74	68	58	87	3.4	2.1	1.3

*From the Department of Medicine (Variety Club Heart Hospital), University of Minnesota Hospitals.

exertion, and two had developed syncope with effort. In no instance was there evidence of congestive heart failure.

The objective physical findings in this group of cases were remarkably similar. A loud systolic murmur with thrill could be heard along the left sternal border in the third intercostal space. The pulmonary second sound was not remarkable. In only one instance was cyanosis or clubbing of the nail beds apparent. The heart was not enlarged on physical examination. In five of the eight cases a distinct precordial bulge was seen.

The laboratory findings of interest included the hemoglobins ranging from 14.0 gm. to 18 gm. per cent. The electrocardiograms uniformly showed right ventricular hypertrophy patterns. Cardiac fluoroscopy in all but one instance showed slight to moderate enlargement of the right ventricle and considerable prominence of the pulmonary artery segment with, however, normal peripheral pulmonary vasculature. In one instance a moderate degree of pulmonary emphysema was also present. In one case only there was considerable dilatation of the left main pulmonary artery branch that is

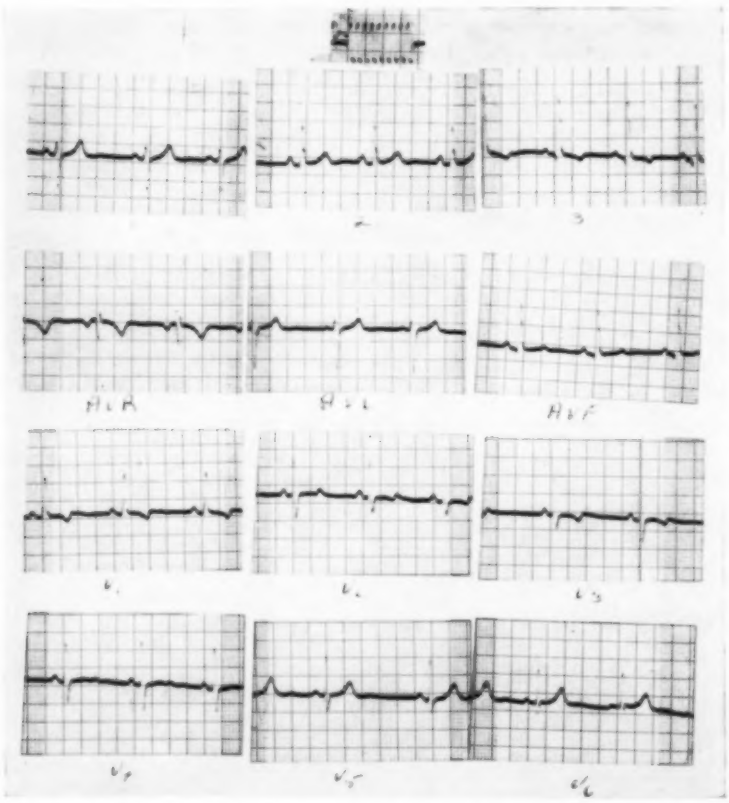

FIGURE 1: Electrocardiogram from patient 1. A right ventricular strain pattern is present.

usually considered to be of the poststenotic type and indicative of pulmonary valvular stenosis. In one other case, the aortic arch was found to be on the right. All of the others presented with a normally situated aortic arch and descending aorta.

Two of the cases are of unusual interest and are summarized as follows:

Case 1: A 26 year old woman was admitted to the hospital with the chief complaint of moderate dyspnea on effort. She was known to have had a heart murmur since birth. Her growth and development, however, had been normal. At the time of her hospital admission, she was employed as a clerk and was able to perform her duties without difficulty. She believed that her fingernails and her lips became blue with moderate exertion and on at least one occasion had fainted when undertaking strenuous effort.

The pertinent physical findings at rest showed minimal clubbing but no cyanosis of the nailbeds. There was a slight pigeon chest deformity. A distinct systolic murmur with thrill could be heard along the left sternal border in the second interspace. The pulmonary second sound was decreased. The peripheral blood pressure was 90/50 mm. Hg. The remainder of the physical examination was within normal limits.

The hemoglobin was 14.1 gm. per cent. The electrocardiogram showed a right ventricular strain pattern (Fig. 1). Cardiac fluoroscopy showed moderate enlargement of the right ventricle and considerable prominence of the pulmonary artery segments especially on the left suggesting a left-to-right shunt and pulmonary valvular stenosis. The peripheral pulmonary vasculature was normal (Fig. 2).

This patient had been catheterized in another hospital, and the pulmonary artery had not been entered. However, the cardiac catheter did pass directly from the right ventricle into the ascending aorta thereby establishing a diagnosis of ventricular septal defect, although there was no evidence of either a left-to-right or any right-to-left shunt at that time from the blood gas analyses. She was recatheterized following her admission here, and on this occasion the pulmonary artery was entered. The data are given in Table I. The evidence for pulmonary stenosis is clear-cut indicating a relatively high degree of pulmonary stenosis. The change in the pressure tracing as the catheter was withdrawn suggested that this stenosis was probably of the valvular type. On this occasion there was quite definite evidence of a left-to-right shunt at probably the ventricular level as revealed by blood gas analyses.

Figure 2: Postero-anterior and left anterior oblique chest films from patient 1. Mild right ventricular enlargement and prominent pulmonary arteries are seen. The arterial markings are reduced in the lung periphery.

It was decided to attempt a completely corrective operation in this case and cardiotomy was undertaken. At operation, a high ventricular septal defect was found measuring 3 x 3½ cm. in size. In addition, there was a bicuspid stenotic pulmonary valve. The ventricular septal defect was closed and the stenotic pulmonary valve was opened under direct vision. Her post-operative course, however, was never satisfactory and she expired on the fourth post-operative day. The autopsy findings were the same as described at the time of operation except that, in addition, an area of infundibular pulmonary stenosis was found.

The second case thought worthy of detailed description was a 53 year old man who first came to the University Hospital at the age of 31 because of conjunctivitis. At that time there was a history of mild dyspnea on effort and cyanosis for as long as

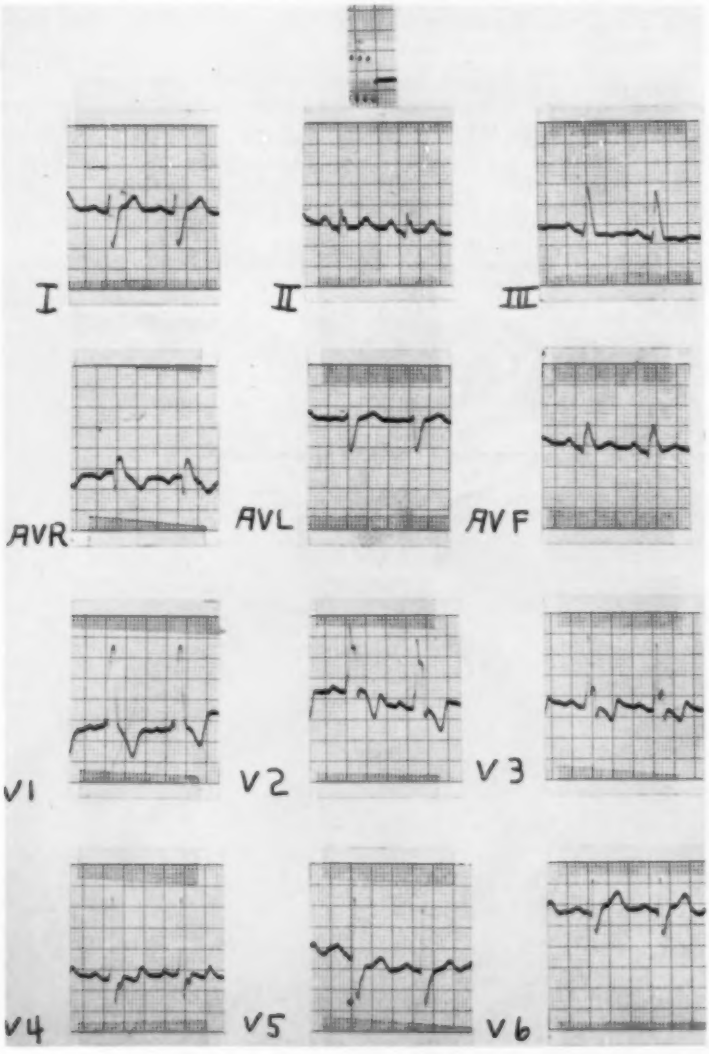

FIGURE 3: Electrocardiogram from patient 8, consistent with right bundle branch block.

he could remember. Examination showed him to be of somewhat smaller than normal stature, with moderate cyanosis of the nailbeds and mucous membranes and with clubbing of the fingers and toes. The vital capacity at that time was 4 liters and the blood pressure was 94/72 mm. Hg. The heart was not enlarged and there was a loud systolic murmur present over the pulmonary region and heart also in other areas of the precordium but with lesser intensity. A distinct systolic thrill was present in this same region. Cardiac fluoroscopy showed enlargement of the right ventricle. An electrocardiogram was interpreted as showing right ventricular preponderance and delayed intraventricular conduction.

This man was not seen again until the age of 53, at which time he came to the Urological Service because of bladder neck obstruction. During the interval he had worked as an accountant. He continued to note dyspnea on effort and occasional aching pain in the anterior aspect of the chest on the left side. He thought that there was a slight increase in his dyspnea and fatiguability recently. Physical examination showed him to be 65 inches tall and to weigh 127 pounds. Blood pressure at that time was 120/80 mm. of mercury. There was marked cyanosis of the tongue. The mucous membranes and nailbeds were also cyanosed, and there was considerable clubbing of the fingers and toes. The lungs were clear on percussion and auscultation. The heart did not appear to be enlarged. A harsh grade IV systolic murmur was once again heard in the pulmonary region, and a systolic thrill was maximal in that area. The pulmonary second sound was decreased. The only other positive physical finding was grade II benign prostatic hypertrophy.

The pertinent laboratory findings included a hemoglobin of 18.6 gm. per cent. The leukocyte count was 5,150 with a normal differential. The blood urea nitrogen was 16 mg. per cent. The electrocardiogram was consistent with right bundle branch block (Fig. 3). Cardiac fluoroscopy showed slight generalized cardiac enlargement. The pulmonary vascular pattern was thought to be normal (Fig. 4).

Cardiac catheterization was carried out and the data are given in Table I (Case 8). The evidence of pulmonary stenosis was clear-cut, and there was a significant increase in the right ventricular and pulmonary artery blood saturations as compared to the right atrium and superior vena cava. In addition, the femoral artery saturation at rest was only 87 per cent. It was thought that the clinical and physiological findings were quite consistent with those of tetralogy of Fallot except that in this instance there was a considerable left-to-right shunt at probably the ventricular level.

Physiological Findings

These are given in Table I. There was, in each instance, considerable evidence of pulmonary stenosis with mean pulmonary artery pressure ranging

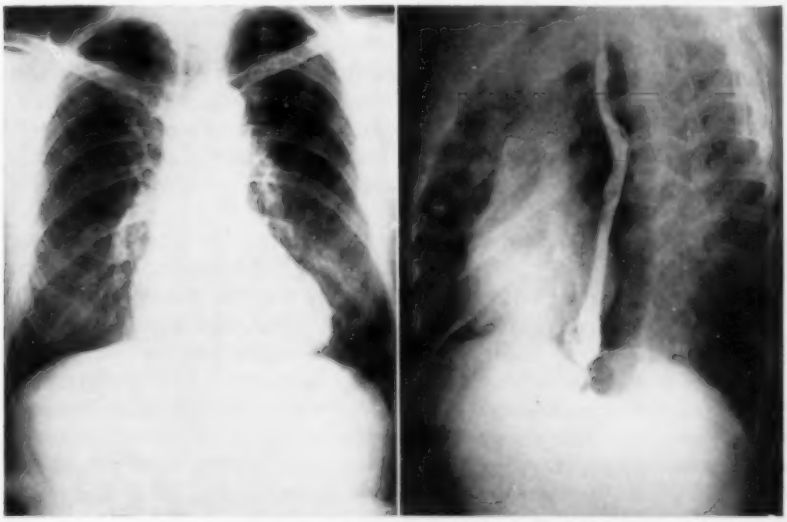

Figure 4: Postero-anterior and left anterior oblique views of the chest from patient 8 showing slight generalized cardiac enlargement and normal lung vasculature.

between 7 and 17 mm. of mercury and the right ventricular systolic pressures ranging from 70 to 138 mm. of mercury. The saturations of the blood within the pulmonary circuit ranged from 74 to 91 per cent and in each instance there was evidence of a left-to-right shunt, the value of this shunt ranging from 1.3 to 6.9 liters/minute. All of the femoral artery samples were normally saturated except for the second case described above (Case 8) whose femoral artery saturation at rest was 87 per cent. The anatomical diagnoses of pulmonary stenosis and ventricular septal defect were proved at autopsy in Cases 1 and 3 and at the time of surgery in Case 2. In the other five instances the diagnosis rests upon the clinical picture plus the roentgen and cardiac catheterization findings.

Discussion

It is apparent from an examination of the eight cases here reported plus their physiological data that this combination of defects can represent a relatively benign situation. All of these people survived to adulthood, and in fact, one was still functional class II at the age of 53 years. This may be related to the fact that the pulmonary stenosis was severe enough to prevent an excessive left-to-right flow, and consequently the development of the unfortunate complications of a simple ventricular septal defect such as an increase in the pulmonary vascular resistance and pulmonary hypertension. On the other hand, the pulmonary stenosis was not severe enough to elevate the right ventricular systolic pressure to the extent that a right-to-left shunt through the ventricular septal defect could occur at rest. For this reason, it would certainly appear to be unwise to simply resect the pulmonary stenosis since one could reasonably anticipate that the left-to-right shunt would materially increase under those circumstances, and it is entirely possible that the patient could become considerably worse if such an operation were successfully carried out. Simple closure of the ventricular septal defect would probably be a satisfactory procedure with such cases although the additional task of resecting an area of pulmonary stenosis at the same time is relatively minor and should certainly be attempted. Actually, the question of surgical intervention in similar cases where there is a relatively small degree of functional impairment of the cardiovascular system can be seriously questioned and, indeed, may be inadvisable unless the patient is having serious difficulty.

The cardiac catheterization studies in this group of patients were carried out at rest. Whether or not a reversal of the left-to-right shunt can occur with exercise is of some importance. Studies with exercise have been done in one instance previously reported and in that case the femoral artery saturation fell from a value of 92.5 per cent prior to exercise to 29.2 per cent after exercise at which time syncope occurred.[1] It therefore appears quite possible that although these cases were all, with one exception, asymptomatic and acyanotic at rest, a moderate to mild degree of arterial oxygen desaturation may occur with physical effort. This has been related to the fact that the pulmonary stenosis imposes a fixed resistance in the lesser circulation. With exercise, the peripheral resistance in the systemic circuit drops by reason of vasodilatation and an increased flow of blood through

the skeletal muscles does occur. The lowering of the systemic pressure under these conditions may well be sufficient to reverse the pressure gradient across the ventricular septal defect and to result in a right-to-left shunt.

Case 8, a 53 year old man, presented clinically as a tetralogy of Fallot. This represents an unusual survival since the mean age at death of a series of 85 cases collected by Maude Abbott was 12 years and 9 months with the oldest surviving patient 36 years.[2] There have been cases of unusual survival such as that of the American musician, John Gilbert, who died at the age of 59 years.[3] A recent report described seven cases from the medical literature that survived 40 years or longer.[4]

The finding of a significant left-to-right shunt in this instance was unexpected but may help to explain his unusual longevity. It is noted that the right ventricular pressure at rest was only 84/3 mm. of mercury. Since this man followed a sedentary occupation, it is unlikely that his peripheral arterial oxygen desaturation has ever been marked although it is significantly reduced at rest. In this case, one might explain the peripheral desaturation not on the basis of a predominant pressure gradient from right ventricle but rather to cyclic variations in the pressure gradient between the two ventricles based upon asynchronism of the pressure curves in the two ventricles. In other words, there may be instantaneous variations in the pressure gradient so that shunting from right-to-left may occur for a brief part of the cardiac cycle although the major pressure gradient is in the opposite direction. It is tempting to assume that the longevity in this instance is related to such a situation, and it is quite possible that catheterization studies in other elderly tetralogies of Fallot might reveal the same hemodynamic pattern.

One serious difficulty is that of a correct designation for this group of cases. From the strictly anatomical point of view, these people present the findings described by Fallot—namely pulmonary stenosis and a ventricular septal defect. There has been considerable discussion of the problem of "over-riding" of the aorta in the case of tetralogy of Fallot and this has, in fact, been advanced as an argument against the attempted closure of the ventricular septal defects in this condition. Recently acquired surgical experience, however, has indicated clearly that true anatomical over-riding of the aorta rarely, if ever, occurs with the tetralogy of Fallot and no difficulty in repairing the ventricular septal defect has been encountered because of malposition of the aorta. To the best of our knowledge the pressure gradient is by all odds the most important factor determining the right-to-left shunt and the position of the aorta is of little or no consequence to the ordinary tetralogy of Fallot.

Anatomically, then, this group of cases does fall into that of the tetralogy of Fallot. Physiologically, however, these people behave in quite a different manner and calling them tetralogy of Fallot or a variant creates a great deal of confusion in clinical discussions. The more precise term, of course, is a descriptive one and that would be pulmonary stenosis, ventricular septal defect, and preponderant left-to-right shunt without cyanosis. This name becomes quite cumbersome for daily usage and the term "acyanotic

tetralogy of Fallot," although not perfect, seems to be adequately descriptive to avoid comment.

With surgical techniques now available, this lesion can be completely corrected. The relatively benign course of the adult patients so far recognized would raise a serious question as to the advisability of surgical interference. These people seem to be able to lead relatively normal lives, to be gainfully employed, and it would not seem reasonable to seriously entertain the idea of surgical correction in view of the relatively high surgical mortality at the present time.

SUMMARY

1. Eight adult cases with pulmonary stenosis, ventricular septal defect, and predominant left-to-right shunt have been studied clinically and physiologically.

2. In only one instance was there cyanosis at rest. This occurred in a man, age 53, who presented clinically as a straight-forward tetralogy of Fallot. The fact that the shunt is still bidirectional may in part account for his unusual longevity.

3. This combination of lesions seems to be relatively benign and to be accompanied by a good prognosis both for functional capacity and long-term survival.

4. This lesion is theoretically and actually completely correctible with surgical techniques now at hand. The risk, however, seems to be excessive at the present time in view of the relatively small degree of functional impairment present in this syndrome.

5. The proper term for designating such cases would seem to be the descriptive one of pulmonary stenosis, ventricular septal defect, and preponderant left-to-right shunt. However, in view of the cumbersomeness of this descriptive title it would seem preferable and permissable to refer to such cases as "acyanotic tetralogy of Fallot."

RESUMEN

1. Ocho adultos con estenosis pulmonar, defectos septales ventriculares, y shunt predominante de izquierda a derecha, se estudiaron clínica y fisiológicamente.

2. En sólo un caso la cianosis era un reposo. Esto occurió en un hombre de 53 años que tenía clínicamente una tetralogía de Fallot-adelantada.

El hecho de que el shunt sea aún bidireccional, puede en parte explicar la inusitada longevidad.

3. Esta combinación de lesiones parece ser relativamente benigna y ser acompañada por buen pronóstico tanto funcional como de sobrevida.

4. Esta lesión en teoría y de hecho es corregible quirúrgicamente con las ténicias actuales. El riesgo sin embargo, parece ahora excesivo en vista del pequeño grado de daño funcional que representa.

5. El término adecuado para designar estos casos sería el de estenosis pulmonar, defecto septal ventricular y shunt preponderante desería preferible y permisible hablar en tales casos de "Tetralogía de Fallot Acianótica."

ZUSAMMENFASSUNG

1. 8 Fälle von Erwachsenen mit Pulmonal-Stenose, Ventrikel-Septum-Defekt und überwiegendem Links-Rechts-Shunt wurden einer klinischen und physiologischen Untersuchung unterzogen.

2. Nur in einem Fall bestand eine Cyanose in Ruhe. Sie lag vor bei einem Mann von 53 Jahren, der klinisch das Bild einer einfachen Fallot' Sohen Tetralogie bot. Die Tatsache, dass der Shunt noch nach beiden Richtungen geht, kommt möglicherweise zum Teil als Ursache für die ungewöhnliche Lebensdauer in Betracht.

3. Diese Kombination von Veränderungen scheint relativ gutartig und mit einer guten Prognose verknüpft zu sein, sowohl hinsichtlich der funktionellen Fähigkeit als auch der Überlebensdauer.

4. Diese Veränderung lässt sich theoretisch und tatsächlich vollständig korrigieren mit der jetzt zur Verfügung stehenden Operationstechnik. Das Risiko scheint jedoch im Augenblick übergross zu sein in Hinblick auf den relativ geringen Grad funktioneller Schädigung, wie sie bei diesem Syndrom auftritt.

5. Die zutreffende Bezeichnung für die Kenntlichmachung solcher Fälle dürfte die rein beschreibende sein, nämlich die einer Pulmonal-Stenose, Ventrikel-Septum-Defekt und überwiegendem Links-Rechts-Shunt. Im Hinblick jedoch auf die Schwerfälligkeit dieses beschreibenden Ausdruckes dürfte es vorzuziehen und erlaubt sein, sich auf solche Fälle als "nicht cyanotische Tetralogie von Fallot" zu beziehen.

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Status Bronchospasticus of Non-Allergic Origin*

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The condition I am about to discuss is characterized by sustained or periodically recurring tonic contraction of the peribronchial and peribronchiolar muscles which is etiologically not related to any allergic factor. Although non-allergic bronchospasm was reported sporadically by early clinicians, even nowadays it is rarely mentioned in medical writings. This condition is far more common than it is generally realized. It occurs from infancy to old age. It may develop in persons with congenital or acquired imbalance of the autonomic nervous system with predisposition to parasympathetic preponderance. In these instances stimuli which cause no pathlogic reaction in normal individuals, induce excitation of the vagus nerve with consequent bronchial spasm. This disorder may be designated as bronchospasmophilia. In other cases, irritation of the vagus nerve is elicited in normal individuals by unusually severe provocative influences.

Causative factors of this condition belong in the following categories:

1. Intrinsic
   - A. Diseases of the Lung
   - B. Heart disease
   - C. Reflex manifestation
   - D. Cough
   - E. Endocrine influences
2. Extrinsic
   - A. Environmental
   - B. Foreign bodies
   - C. Reflex
   - D. Iatrogenic
   - E. Smoking
3. Cough
4. Psychogenic

There are great variations in the development and course of this condition. Its onset may begin with irrevelant symptoms easily disregarded by the patient. In others, sudden, severe symptoms may be disturbing, even alarming. In early cases, episodes of bronchospasm may alternate with long, symptom-free intervals. When the disease runs a mild course, the patient is likely to become habituated to his predicament. This condition is rare in pregnancy.

Bronchospasm may be diffuse, bilateral or it may be lobar, segmental or regional in extent.

Pulmonary disease, acute or chronic, may be associated with this type of bronchoconstriction. In addition to mechanical irritation of vagal nerve endings by mucosal swelling, catabolic products of inflammation, including histamine and lactic acid liberated from destroyed leukocytes may cause it. Bronchospasm may be localized, regardless of its origin from a great variety of parenchymal, interstitial or bronchial forms of lung disease, in the region of involvement, it may be in distant parts of the same lung or on the opposite side.

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Dyspnea and cough are often overlooked as manifestations of bronchospasm in heart disease. Bronchospasm resulting from pulmonary stagnation is a major factor in the syndrome known as cardiac asthma. The type of dyspnea seen in the latter is similar to that observed in bronchial asthma. Cardiac asthma may be conditioned by environmental influences, by mental and emotional tension as well as by fatigue.

Bronchospasm is frequently encountered as a result of a reflex which may originate from extrapulmonary areas innervated by the vagus nerve or through direct or indirect transmission of nerve impulses from the pleura, mediastinum, chest wall or the diaphragm. Thus undue distention of the stomach, intestines and gall bladder may be associated with bronchospasm. The occurrence of bronchospasm secondary to major abdominal operations, particularly in the upper abdominal region, is a well established fact. The most common cause of reflex bronchospasm is irritation of the upper respiratory tract.

It is well to emphasize the possibility of inducing or aggravating bronchospasm inadvertently by therapeutic intervention. In addition to pilocarpine, physiostigmine and prostigmin, mention should be made of morphine and digitalis. Also, it is known that topical application of cocaine in the upper air passages, prior to diagnostic studies, may exert the same adverse influence. Vigorous diuresis induced in patients with heart failure may result in hyperpotassemia (hyperkalemia). The latter favors the liberation of acetylcholine which, in turn, stimulates parasympathetic nerve endings.

Tobacco smoking, through inhalation or swallowing of nicotine, may result in bronchospasm in three ways: 1. by acetylcholine-like action of nicotine; 2. by causing bronchitis; 3. by chronic coughing provoked by irritation of the air passages.

One of the possible harmful effects of cough, bronchospasm is brought about by stretching of the bronchial mucosa during strenuous coughing. Also, hypoxia resulting from excessive coughing may irritate vagal nerve endings so as to cause bronchial constriction.

Bronchoscopic observations show that adverse emotional impressions cause bronchospasm. Experimental investigations prove that stress causes hyperkalemia. The latter leads to an increase in acetylcholine at the nerve endings of the autonomic nervous system. In individuals who belong in the category of bronchospasmophilia, undue mental and emotional stress and strain may serve as provocative causes of bronchospasm. This response is analogous to cardiospasm and pylorous spasm in persons with vagotonia. Possibly, the term homo sapiens can be aptly augmented by the term "homo leiomyospasticus."

Various gradations of bronchospasm result in proportionate interference with bronchial peristalsis and normal bronchocatharsis. With this bronchial dysrhythmia (dyskinesia), there is likely to be stagnation and retention of pathogenic micro-organisms, atmospheric pollutants, carcinogens, inflammatory exudate, transudate and extravasated blood. I have seen a great many instances of emphysema of bronchospasmogenic origin.

Oftentimes, one finds evidence of localized (regional) emphysema which

is limited to a lobe, to a segment or subsegment. Bronchospasm may be the explanation of pulmonary bullae and subpleural blebs with possible interstitial emphysema, pneumomediastinum and spontaneous pneumothorax.

Atelectasis of various extent results from complete occlusion of a regional bronchus by spasm. As a rule this type of atelectasis is transient. In lung units smaller than a lobe, atelectasis is conditioned by closure of interalveolar pores of Kohn. Dyspnea more severe than would correspond to the extent of atelectasis is explained by disturbance in the cycles of the Hering-Breuer reflex.

The right ventricle of the heart may be adversely affected by bronchospasm: 1. by pulmonary vasoconstriction due to hypoxia; 2. by increased resistance in the lesser circulation due to alveolar pneumatic hypertension.

Bronchospasm begets bronchospasm. Prolonged periods of recurrent bronchospasm result in hypertrophy of the peribronchial smooth muscles. Bronchospasm is accompanied by reduced respiratory motions of the diaphragm.

One or more of the following symptoms are observed in bronchospasm: wheezing, dyspnea, cough and chest pain. Symptoms may be slight, annoying, even distressing. They may be aggravated by physical exertion, premenstrual tension and other endogenous influences. Wheezing and dyspnea may be nocturnal.

Bronchospasm may have its inception in senescence. In such cases, when the condition is severe enough to result in prolonged hypoxia, the patient may complain of headache, giddiness, loss of appetite, nausea, diminished hearing, weakness, tiredness, insomnia, tremor, tachycardia or he may have episodes of disorientation and hallucination.

Diagnostic studies should evaluate history, symptoms, personality, objective signs, physical, X-ray and laboratory findings, function studies, therapeutic tests and if necessary, bronchoscopic observations.

In generalized bronchospasm the percussion note is hyperresonant. Sibilant and sonorous rales are audible over both lungs. Fluoroscopic and roentgenographic examinations show distention and limitation in motion of the thoracic cage. The diaphragm occupies a low position and its excursions are limited. Radiotranslucency of the lung is increased. Regional bronchospasm presents proportionately smaller changes. Bronchograms are of value in such cases.

The cardinal aim of treatment is to restore the normotonic (eutonic) status of the peribronchial and peribronchiolar smooth muscles. Of the bronchospasmolytic drugs isopropyl epinephrine has been found of superior value in my experience. It is available under a number of proprietary names. Closely related compounds are neosynephrine and butanephrine. Ephedrine and several ephedrine-like chemicals are suitable for inducing satisfactory relaxation of spastic bronchi. Theophylline with ethylenediamine is a remarkably efficacious bronchospasmolytic drug. My results with a number of anticholinergic preparations (parasympathetic blocking agents) have been highly satisfactory. I prefer the administration of diethylmethylammonium bromide (antrenyl bromide).

Atropine, scopolamine and similar drugs should be used with circumspection because of their possible untoward effects upon the bronchial mucosa.

Patients under close observation may be given prednisone or prednisolone. Their bronchospasmolytic action is impressive, indeed.

All these measures are reviewed with the premise that competent care and treatment of coexistent cardiopulmonary disease are handled expeditiously and that due attention is paid to concurrent mental and emotional problems of the patient which, directly or indirectly may have causal connection with bronchospasm.

SUMMARY

1. Attention is focused on the ubiquitous prevalence of bronchospasm of non-allergic origin.

2. The main causative factors of this condition are enumerated, with commentary on the role of various lung diseases, heart failure, cough, extraneous environmental factors, psychogenic influences and reflex irritation of the peribronchial smooth muscles from extrapulmonary sources.

3. Adverse sequels of non-allergic bronchospasm are discussed, with particular reference to wheezing, dyspnea, cough, chest pain, tussive insufficiency and pseudohypertrophic emphysema.

4. The cardinal aim of treatment is to restore the normotonic (eutonic) status of the peribronchial and peribronchiolar smooth muscles. Adequate treatment of the underlying provocative condition is emphasized and the author's favorable clinical experience is recorded, with bronchospasmolytic and anticholinergic drugs and with corticosteroids.

RESUMEN

1. Se enfoca la atención sobre la ubicuidad del broncoespasmo en padecimientos no alérgicos.

2. Las causas principales se enumeran comentando el papel que tienen varias enfermedades pulmonares, insuficiencia cardiaca, tos, factores extraños del ambiente, influencias psicógenas, y la irritación refleja de los músculos lisos peribronquiales desde fuentes extrapulmonares.

3. Se discuten las secuelas más adversas del espasmo bronquial no alérgico especialmente en lo referente a silbidos traqueales, disnea, tos, dolar torácico, insuficiencia de la tos y enfisema seudohipertrófico.

4. El objetivo principal del tratamiento es la restauración de la condición normotónica (eutónica) de los músculos peribronquiales y peribronquiolares. El tratamiento adecuado de la afección subyacente provocadora se recalca y se relata la experiencia favorable del autor con el uso de drogas broncoespasmolíticas, anticolinérgicas y con los corticosteroides.

RESUME

1. L'auteur attire l'attention sur l'importance et la fréquence du bronchospasme non allergique.

2. Il énumère les principaux facteurs de cet état, il commente le rôle des différentes affections pulmonaires, de l'atteinte cardiaque, de la toux,

des facteurs extrinsèques, des influences psychogéniques, et de l'irritation réflexe des muscles lisse péribronchiques d'origine extrapulmonaire.

3. Les auteurs discutent les conséquences du bronchospasme non-allergique en insistant particulièrement sur le wheezing, la dyspnée, la toux, la douleur thoracique, l'emphysème pseudo-hypertrophique tussigène, et facteur d'insuffisance fonctionnelle.

4. Le point le plus important du traitement est de restaurer l'état normotonique (eutonique) des muscles lisses péribronchiques et péribronchiolaires. L'auteur indique le traitement convenable de la cause provocante et fait part de l'expérience qu'il a pu acquérir en utilisant les médications bronchospasmolytiques et anticholinergiques ainsi que les corticostéroïdes.

ZUSAMMENFASSUNG

1. Es wird die Aufmerksamkeit gelenkt auf ein ubiquitäres Vorkommen des Bronchospasmus nicht allergischen Ursprunges.

2. Es werden die wesentlichen ursächlichen Faktoren für diesen Zustand aufgezählt mit Erläuterung der Rolle der verschiedenen Lungenkrankheiten Herzschwäche, Husten, fremde Unweltfaktoren, psychogene Einflüsse und reflektorische Reizung der peribronchialen glatten Muskulatur aus extrapulmonalen Quellen.

3. Ungünstige Auswirkungen des nicht allergischen Bronchospasmus werden besprochen unter besonderem Bezug auf Giemen und Pfeifen, Dyspnoe, Husten, Brustschmerzen, Hustenschwäche und pseudohypertrophen Emphysem.

4. Das cardinale Behandlungsziel besteht darin, den normotonischen (eutonischen) Status der peribronchialen und peribronchiolaren glatten Muskulatur wieder herzustellen. Angemessene Behandlung der zugrundeliegenden Krankheitsursache wird besonders betont, und es wird berichtet über die günstigen klinischen Erfahrungen des Verfassers mit Mitteln zur Lösung des Bronchospasmus, anticholinergischen Mitteln und mit Corticosteroiden.

Ambulatory Pneumoperitoneum on Chinese*

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Ambulatory pneumoperitoneum was given from one month to eight years in 1031 cases of pulmonary tuberculosis among Chinese. Some of them (5 per cent) received air one to four times only and stopped treatment because of initial discomfort and pain experienced, and/or due to the influence of others, laymen and medical. It was only during the past two decades, more particularly after World War II, that the Chinese gradually became aware of and acquainted with the universal orthodox methods of treating tuberculosis. Pneumoperitoneum, though simple in experienced hands, first made its appearance in Hong Kong and Canton in 1941. It was not fully appreciated as a safe orthodox method of treatment for pulmonary tuberculosis by the medical profession here until after World War II. The energetic efforts of the local Anti-Tuberculosis Association in tuberculosis education through the radio, newspapers, schools, printed pamphlets, mass x-ray film inspection of employees and students; the establishment of a conveniently situated tuberculosis center, free hospitals and clinics; the the constant drive for much needed funds to carry on the work and finally, the ease of accessibility to foreign modern equipment, literature, and the available well trained personnel in the past few years (five to be more exact), have contributed much in opening the eyes of the local populace toward the beneficial effects of modern methods of treatment. Here, today, pneumoperitoneum has become one of the established conventional methods of collapse therapy. Indeed, it has gradually displaced pneumothorax in our clinic. Our experience has convinced us of the various well known complications (pleural effusions, empyema, broncho-pleural fistulas, thickened pleuras, mediastinal shifts, unexpanded lung, etc.) of pneumothorax, and the lack of serious complications (few and rare) of pneumoperitoneum, to the extent that lately we have used the latter exclusively to initiate collapse therapy when this treatment was indicated. Up to 1948 pneumothorax had been attempted on all suitable cases for collapse therapy on one or both sides, and it was only on failing to establish a good collapse after one month or more or following failures after two or more trials that pneumoperitoneum was resorted to. In the past five years there has been an increasing number of cases in our clinic receiving pneumoperitoneum without having had pneumothorax tried. The encouraging good results with so few complications were so convincing that since December 1952, all cases suitable for collapse therapy received pneumoperitoneum as initial treatment exclusively.

The value and importance of isolation with a reasonable period of sanitorium treatment is indisputably the best treatment for the tuberculosis

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patient. The lack of free beds and the poor economic status of our patients together with the prevalent instinct, attitude and tendency of the public to ostracize the known infected, have forced us to resort to ambulatory treatment. In the British colony of Hong Kong with a population of 2,250,000 there are only 928 more or less free beds for the treatment of tuberculosis. Ninety per cent of our patients receive low wages, living from day to day. These are comprised of bookkeepers, sales clerks, fokis (helpers and errand boys of shops, stores, offices, etc.), street hawkers and vendors, barbers, waiters, factory workers and others of the low salary group. The average patient earned from three to 10 Hong Kong dollars a day (one United States dollar is equivalent to six Hong Kong dollars), providing bare livelihood in the lowest of standards, with a poor diet, and living in much congested quarters. Though infection is universal, the patient lives in constant fear of having others know the true nature of his disease, for his friends, neighbors and other contacts (social and otherwise) would tend to avoid him. Known as a chest clinic dealing more or less exclusively with tuberculosis, we do have the occasional patient of the upper social status, who is bold and daring enough to be seen in our office a number of times. To have tuberculosis is to be a social outcast. Finally, hospitalization even if it were financially possible for any length of time would ensure disclosure of one having the much dreaded disease, which would eventually lead to much inconvenience and embarrassment, and at times, loss of employment. A reasonable practical solution had to be found, which would enable the patient to resume his former employment with minimum loss of time and least embarrassment to his social status. We have had to resort to ambulatory treatment, and the use of pneumoperitoneum as the type of collapse therapy conveniently and satisfactorily applicable in this environment.

We have insisted on, and still do, admission of all patients to St. Paul's Hospital (a semi-charity institution) for a minimal period of three to 10 days. We have found it much more expedient to concentrate our work in one particular institution, where the staff is sympathetic, congenially encouraging to the patients, and easily adapted to our methods. During the brief period of hospitalization, pneumoperitoneum was given one to three times, bed rest observed for the first day at least, to avoid any possible discomfort and serious complications; and advice was given to impress the necessity of personal hygiene and individual precautions, both in avoiding future exposure to added infections and infecting others. Special attention was focused on the cough and the proper disposal of sputum.

Initially 500 cc. of air was usually given, 800-1000 cc. two or three days later, and 1200-1500 cc. four days subsequently. Refills of 1500 to 2000 cc. air each time after discharge were gradually spaced to 10, 12, 14, 18, and the most, 21 days, which was usually attained after three to four months' treatment. The long intervals (14 to 21 days) between refills were made for the patients' convenience, in that too much time would not be taken away from their work. For the most part, frequent and small refills were given whenever possible. Fluoroscopy was done before every third refill

or whenever indicated, and an x-ray film taken three months after initial pneumoperitoneum and subsequently at six months' interval or whenever there was an indication as shown on fluoroscopy or otherwise.

General Discussion and Analysis of the 1031 Cases

Sex. Of the 1031 cases, 740 (71.8 per cent) were males, an approximate ratio of 4 to 1 (Table IA).

TABLE IA

	MALE		FEMALE	
Stage	Number	Percentage	Number	Percentage
I	176	17.1	69	6.7
II	143	13.9	47	4.5
III	421	40.8	175	17.0
TOTAL	740	71.8	291	28.2

The predominance of males was partly due to greater percentage of tuberculosis in the group and partly due to the tradition of the Chinese people's preference to take care of the men folks.

Age. The greatest number of cases were found in the age group 21-40 years (727 or 70.5 per cent), the most productive period in a man's life, and the greatest number of consultations also appeared in this group. There were 115 (11.1 per cent) in the 15-20 years group, 139 (13.5 per cent) in the 41-50, and only 50 cases in the 51-70 years group (Table IB).

TABLE IB

AGE	CASES	PERCENTAGE
15 - 20 years	115	11.1
21 - 30 years	422	40.9
31 - 40 years	305	29.6
41 - 50 years	139	13.5
51 - 70 years	50	4.9

Extent of Disease. Five hundred and ninety-six (57.8 per cent) cases were far advanced, 190 (18.4 per cent) moderately advanced and 245 (23.8 per cent) minimals (Table IC). In the earlier years, between 1941 and 1947, 85 to 90 per cent of our cases were far advanced. More minimal cases were discovered through case finding surveys in the later years (1948-1953). An increasing number of minimal lesions have appeared for treatment each year with the result that now there are more early than advanced cases.

Tuberculosis with Asthma. Nine had bronchial asthma with pulmonary tuberculosis. Two of these had pneumoperitoneum for two and a half years, and had discontinued treatment for one and two years respectively. Their

TABLE IC

STAGE	CASES	PERCENTAGE
I	245	23.8
II	190	18.4
III	596	57.8

tuberculosis has been inactive since, but they still have the occasional asthmatic attacks though less frequent and less severe. Two are still receiving pneumoperitoneum, one for two and a half years, the lesion being inactive for two years, and the other for one year and the tuberculosis had spread. The asthmatic attacks in both cases have been less severe and less frequent. Pneumoperitoneum was discontinued in one case after six months because the asthma was aggravated with treatment, and improvement was noted both in the tuberculosis and asthma when put on dihydrostreptomycin (DHS) and isonicotinic acid hydrazide (INAH) intermittently. There were no results noted in two cases because follow up was not possible, and two died of malnutrition after one month of treatment. It is our impression that pneumoperitoneum has its place in the treatment of asthma with tuberculosis even though the number of our cases is small.

Tuberculosis with Emphysema. Pneumoperitoneum was given in two cases of emphysema; one for 26 months, and observation continued in the following six months showed complete relief of symptoms; while the other patient showed definite improvement after six months treatment. Of the 10 cases with tuberculosis and emphysema, five died of malnutrition after one to six months' treatment, three discontinued because symptoms were worse after one to two months, no record of one case who had only three refills and stopped coming back, and one was free of symptoms after two and one-half years of pneumoperitoneum with one and a half years follow-up. Apparently with good nutrition, pneumoperitoneum has an important and favorable place in the treatment of emphysema with or without tuberculosis.

Basal Lesions. The 30 cases of basal lesions (Table II) showed definite improvement with fibrosis or closure of cavities with fibrosis resulting in inactive lesions with pneumoperitoneum given six months to four years in 16 patients, improvement on film shadows with absence of symptoms and sputum still positive in four, symptoms improved in three, and the condition showed no changes in seven. Patients who had improved a little or not at all were those in which treatment was not kept up long enough. Only two of these continued pneumoperitoneum for over five months, and two had phrenic crush while one had evulsion. With patience and co-operation between the patient and doctor, pneumoperitoneum, in our opinion, is the preferred therapeutic measure in basal lesions.

Miliary Tuberculosis and Other Complications. Three miliary tuberculosis cases were treated with chemotherapy as well (DHS and INAH), and though the lungs became clear after three to eight months, they subse-

TABLE II

	Cavities	Thickened Pleura	Pleurisy with Effusion	Basal Lesions	T. B. Laryngitis	
					F.	M.
Right	252	83	12	8		
Left	122	71	11	4	7	22
Bilateral	410	15	0	18		
TOTAL	784	169	23	30		

quently died of tuberculous meningitis.

Twenty nine had tuberculous laryngitis. The great majority of them were seen before World War II. Since the wide use of streptomycin in the colony there has been a gradual decline, and only two cases were seen in 1953 in our clinic.

Further analysis showed three had anal fistula; 784 had cavities measuring over 1 cm. in diameter or honey-combing; 169 with thickened pleura; and 23 had pleurisy with effusion as well.

Pregnancy. Pregnancy occurred 14 times. Pneumoperitoneum was continued in all cases up to the seventh or eighth lunar month, with gradual decrease of air given as the pregnancy progressed.

Treatment was resumed one to two weeks following delivery. While we did not encourage conception, we made every effort to continue pneumoperitoneum as long as possible in our pregnancy cases and re-instate the treatment after delivery.

TABLE III

Side	Phrenic Nerve Operation		Pneumothorax		Hernia		Abdominal Effusion	Abdominal Adhesion	Pregnancy
	Evulsions	Crush	Failed	Continued	Femoral	Inguinal			
Right	44	32	138	6	3	4			
Left	10	27	68	2	2	2	11	8	14
TOTAL	54	59	206	8	5	6			
	113		214		11				

Phrenic Operations. Phrenic nerve operation was done in 113 cases, 54 evulsions and 59 crushes. Most of these were performed on the second to the 10th month of pneumoperitoneum, when it was felt that paralysis of the diaphragm would be an added beneficial adjunct. The great majority (85 per cent) received the operation because we felt they were far advanced and would not continue their pneumoperitoneum for any length of time, and in which case, the operation would be of some benefit. Evulsion was performed in these cases. In the past five years we have preferred phrenic crushes and recrushes whenever necessary. This was due to the greater number of early cases and the increasing number of patients willing to continue pneumoperitoneum for a longer period.

Indications, Contra-Indications and Complications

It is to be noted that we have given ambulatory pneumoperitoneum on Chinese with the various types of lesions as shown above. We are in complete agreement with Banyai, Trimble et al., Menedez, Netzer, Stein and others, more or less on the indications and contra-indications. However, with regard to complications, we wish to report our findings.

Hernia. In spite of attempts to control the hernia with trusses, pneumoperitoneum had to be sacrificed in ten out of eleven cases. Of the 11 hernia cases, 10 were in males, six inguinal and four femoral, and one woman still

receiving refills, has a femoral hernia, which is small and made asymptomatic with a truss. In eight cases, the hernia was first noticed after four to eight months' treatment, two after one year and one after two years. In six however, the tuberculosis was inactive at the time of discontinuance of treatment and have remained inactive during eight to 16 months' observation.

Air Embolism. Accidents, though rare, did happen in nineteen of our patients. These had severe pain, shock and air embolism. One died within five minutes and another in 13 hours. Fifteen survivals refused further refills, though they had been under pneumoperitoneum for eight to 19 months. Undoubtedly a number of air embolism cases with minor symptoms were not noticed as such.

Intra-abdominal Hemorrhage. One had massive hemorrhage in the abdominal cavity three hours following a refill and on laparotomy no bleeding point was found after removing 1000 cc. blood from the abdominal cavity.

Effusion. Small abdominal effusions, which appeared and disappeared, were frequently seen on fluoroscopy. There were 11 cases with large amounts which gave persistent constitutional symptoms. These occurred in nine far advanced and two moderately advanced cases, and where the general nutrition was poor. Clinically, there was always some generalized edema, more prominent in the lower extremities and abdominal distention with loss of appetite, nausea, vomiting and slight fever, requiring specific treatment. Aspirations of 1000 to 3000 cc. fluid (one to five times) were done on these patients; and who were also put on diuretics and given better nourishment (stress made on high protein, vitamins, and liver). The fluid was always light amber, with a high cellular count, eosinophils and lymphocytes predominating, and bacteriological studies were always negative. Pneumoperitoneum was continued in eight cases without further fluid formation after two to six weeks of treatment. Two died with malnutrition and the other did not return for further treatment. It is our impression that poor nutrition was an important contributing factor in massive fluid formation in our cases.

Adhesions. Adhesions of any importance between the diaphragm and abdominal viscera were noted in eight cases, one with minimal, two with moderately advanced and five with far advanced lesions. The most frequent site was at the medial portion of the right diaphragm, where sometimes as much as one-third of its width was adherent to the liver. Splenic and stomach adhesions (strands) were next in their respective order of frequency. In no case were the adhesions serious. Pneumoperitoneum was effectively continued in all.

Deaths

We are certain that a number of the patients who dropped out from observation must have died. Many of them were far advanced and moribund when last seen. The 54 cases of whose deaths we have knowledge, are classified as follows:

TABLE IV
NUMBER OF DEATHS IN PNEUMOPERITONEUM CASES

Cause	Number
Unknown	15
T.B. Pericarditis	1
Hemoptysis	16
Malnutrition	9
Progressive disease	2
Cerebral embolism following extrapleural pneumonolysis	2
Air embolism	2
Spontaneous pneumothorax and empyema	2
Carcinoma	1
Meningitis	3
Bronchopneumonia	1
TOTAL	54

Observation and Results

Patients who discontinued pneumoperitoneum against medical advice. The number in this group (Table V) was quite large (624) because (1) pneumoperitoneum was comparatively new here, (2) good results entailed years (three to five years) of persistent frequent refills, (3) the difficulty in most instances to convince the average Chinese, who has great faith in herbs and drugs, that pulmonary tuberculosis could be cured with the mechanics of collapse therapy by introducing air into the abdominal cavity where no disease was present, and little or no medications needed, and finally, (4) the majority of the cases were far advanced.

TABLE V
PATIENTS DISCONTINUED PNEUMOPERITONEUM AGAINST MEDICAL ADVICE

MONTHS		1 - 3	4 - 6	7 - 12	13 - 18	19 - 24	25 and Over	TOTAL			
								No.	Per Cent	No.	Per Cent
Stage*	Sex										
I	M	55	22	8	4	2	1	92	14.7	120	19.2
	F	22	4	1	0	0	1	28	4.5		
II	M	44	10	7	5	1	7	74	11.8	95	15.2
	F	11	3	7	0	0	0	21	3.4		
III	M	157	50	32	16	14	17	286	45.9	409	65.6
	F	59	19	21	10	7	7	123	19.7		
TOTAL	No.	348	108	76	35	24	33	624	100	624	100
	%	55.8	17.3	12.2	5.6	3.8	5.3				

*According to National Tuberculosis Association Classification of 1950, Diagnostic Standard.

TABLE VI
RESULTS: PATIENTS DISCONTINUED PNEUMOPERITONEUM AGAINST MEDICAL ADVICE

Results*		0	1	2	3	4	5	TOTAL No.	TOTAL Per Cent	No.	Per Cent
Stage	Sex										
I	M	35	19	15	23	0	0	92	14.7		
	F	15	3	3	5	1	1	28	4.5	95	15.2
II	M	26	15	20	12	0	1	74	11.8		
	F	6	5	8	1	1	0	21	3.4	95	12.5
III	M	147	44	69	23	1	2	286	45.9		
	F	55	25	34	6	0	3	123	19.7	409	65.6
TOTAL	No.	284	111	149	70	3	7	624	100	624	100
	%	45.5	17.8	23.9	11.2	0.5	1.1				

**Results:* According to National Tuberculosis Association Classification of 1950, Diagnostic Standard.

Column (0) No improvement or condition unchanged.
Column (1) Symptoms improved.
Column (2) Symptoms improved with some favorable x-ray changes.
Column (3) Inactive for 6 months.
Column (4) Inactive for 12 months.
Column (5) Inactive for 24 to 36 months.

TABLE VII
PNEUMOPERITONEUM DISCONTINUED UNDER MEDICAL ADVICE

Months		1 - 3	4 - 6	7 - 12	13 - 18	19 - 24	25 - 36	37 and Over	TOTAL No.	TOTAL Per Cent	No.	Per Cent
Stage	Sex											
I	M	2	4	13	4	3	6	1	33	26.2	51	40.5
	F	3	4	4	2	1	2	2	18	14.3		
II	M	1	1	2	2	1	4	7	18	14.3	23	18.2
	F	0	0	0	0	2	2	1	5	3.9		
III	M	10	0	5	2	4	11	6	38	30.2	52	41.3
	F	4	0	2	3	2	1	2	14	11.1		
TOTAL	No.	20	9	26	13	13	26	19	126	100	126	100
	%	15.9	7.2	20.6	10.3	10.3	26.6	15.1				

Thirty-five patients had thoracoplasty after receiving air from four to 24 months. The reason for continuing refills for such long periods in some cases was because of the far advanced lesions, while in others, it was difficult to convince them of the necessity to undergo an operation even though there had been marked symptomatic improvement under pneumoperitoneum.

The results in this group (Table VIII) are good as expected, where persisted and prolonged treatment bore fruit. Again the far advanced cases raised the percentage of column 0, the unimproved, while symptomatic improvement was noted in three, improved symptoms with some favorable x-ray film changes in 20. There were eight inactive cases for six months, 36 for one year, and 41 for two to three years. The inactive cases totaled 85 (67.4 per cent).

TABLE VIII
RESULTS: PNEUMOPERITONEUM DISCONTINUED UNDER MEDICAL ADVICE

Results*		0	1	2	3	4	5	TOTAL No.	TOTAL Per Cent	No.	Per Cent
Stage	Sex										
I	M	1	0	1	4	14	13	33	26.2	51	40.5
	F	3	0	0	0	6	9	18	14.3		
II	M	0	1	2	2	5	8	18	14.3	23	18.2
	F	0	0	0	0	2	3	5	3.9		
III	M	10	2	11	1	7	7	38	30.2	52	41.3
	F	4	0	6	1	2	1	14	11.1		
TOTAL	No.	18	3	20	8	36	41	126	100	126	100
	%	14.3	2.4	15.9	6.3	28.6	32.5				

*See Footnote, Table VI.

TABLE IX
PNEUMOPERITONEUM CASES STILL RECEIVING REFILLS

Months		3	4 - 6	7 - 12	13 - 18	19 - 24	25 - 36	37 and Over	TOTAL No.	TOTAL Per Cent	No.	Per Cent
Stage	Sex											
I	M	0	13	20	7	3	8	0	51	18.1	74	26.3
	F	0	6	8	4	4	1	0	23	8.2		
II	M	2	9	15	8	4	8	5	51	18.1	72	25.6
	F	2	2	6	2	1	6	2	21	7.5		
III	M	10	10	28	17	8	19	5	97	34.5	135	48.1
	F	3	6	5	6	9	8	1	38	13.6		
TOTAL	No.	17	46	82	44	29	50	13	281	100	281	100
	%	6	16.4	29.2	15.7	10.3	17.8	4.6				

Table XI is a summation of the results of our 1031 cases of ambulatory pneumoperitoneum, the addition of the figures in Tables VI, VIII and X. The overall shows 303 cases (29.4 per cent) with no improvement, 116 (11.3 per cent) improved symptomatically, 269 (26 per cent) have symptoms improved and x-ray film improvement as well, 255 (24.7 per cent) inactive for six months, 40 (3.9 per cent) for one year, and 48 (4.7 per

TABLE X
RESULTS: PNEUMOPERITONEUM CASES STILL RECEIVING REFILLS

Results*		0	1	2	3	4	TOTAL No.	TOTAL Per Cent	No.	Per Cent
Stage	Sex									
I	M	0	0	3	48	0	51	18.1	74	26.3
	F	1	0	0	22	0	23	8.2		
II	M	0	1	12	37	1	51	18.1	72	25.6
	F	0	0	6	15	0	21	7.5		
III	M	0	1	49	47	0	97	34.5	135	48.1
	F	0	0	30	8	0	38	13.6		
TOTAL	No.	1	2	100	177	1	281	100	281	100
	%	0.35	0.7	35.6	63	0.35				

*See Footnote, Table VI.

TABLE XI
RESULTS PNEUMOPERITONEUM DISCONTINUED AGAINST AND WITH MEDICAL ADVICE, AND THOSE STILL RECEIVING REFILLS

Results*		0	1	2	3	4	5	TOTAL No.	TOTAL Per Cent
	Stage								
	I	55	22	22	102	21	23	245	23.8
	II	32	22	48	67	9	12	190	18.4
	III	216	72	199	86	10	13	596	57.8
Grand Total	No.	303	116	269	255	40	48	1031	100
	%	29.4	11.3	26	24.7	3.9	4.7		

*See Footnote, Table VI.

cent) for two and more years. This makes a total of 343 (33.3 per cent) inactive cases for six and more months. These figures indicate that ambulatory pneumoperitoneum in our hands during the past 13 years was an important, reliable and effective form of treatment on Chinese tuberculosis patients. The ease of induction and refills, the lack of complications, its reversibility together with the ultimate good results indicated above are some of the contributory factors, which made pneumoperitoneum so popular with us, and finally attained the high and respected position in our work today.

Chemotherapy

Chemotherapy was intentionally withheld in our practice until studies were made on the various drugs popularly used. We wanted to know more of the action, complications, dosage, best method of administration, suitable cases and length of time to be used, reasonably expected results, etc., of the individual drugs. The cost was also an important factor, as the great majority of our cases were of low economic level. Some had had one or more of the drugs at one time or another, before coming to us. These had

TABLE XII
PNEUMOPERITONEUM CASES WHICH HAD CHEMOTHERAPY

Months	1 - 3							4 - 6							7 - 9							10 - 12							
Results*	0	1	2	3	4	5	Total	0	1	2	3	4	5	Total	0	1	2	3	4	5	Total	0	1	2	3	4	5	Total	Total
Medicine																													
Dihydro-streptomycin	3	4	6	1	0	2	16	0	0	3	0	0	1	4	0	0	2	0	0	0	2	1	0	1	0	0	1	3	25
Dihydro-streptomycin with Isoniazid	10	11	7	17	1	1	47	1	2	7	29	7	1	47	0	0	2	25	2	1	30	0	1	3	18	0	0	22	146
Streptopas	1	0	2	1	0	0	4	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
Streptopas with Isoniazid	0	1	0	1	0	1	3	0	0	2	0	0	0	2	0	0	0	3	0	0	3	1	0	1	1	0	0	3	11
Isoniazid	19	3	3	4	0	0	29	5	0	8	10	3	4	30	0	0	1	3	0	0	4	2	0	19	25	9	7	62	125
TOTAL	33	19	18	24	1	4	99	7	2	20	39	10	6	84	0	0	5	31	2	1	39	4	1	24	44	9	8	90	312
				99							84							39							90				

*See Footnote, Table VI.

no definite, systematic medical advice. It was not until May 1952 that we began to prescribe chemotherapy for some of our pneumoperitoneum cases systematically.

Results. Table XII shows the results of chemotherapy in some of our ambulatory pneumoperitoneum cases. These were included in our 1031 cases. They are analyzed according to the number of months each drug or combination of drugs taken. The number (25) which had dihydrostreptomycin alone was much too small to enable us to draw any conclusion. The dihydrostreptomycin and isoniazid combination consisted of 146 cases, which took the drugs one to three months, four to six months, seven to nine months, and 10 to 12 months, and are analyzed as such.

This study shows that a great majority of the patients receiving pneumoperitoneum who had isoniazid were benefited, and the combination of dihydrostreptomycin and isoniazid gave even better results. No attempt is made to compare these figures with the cases receiving pneumoperitoneum alone due to the predominance of far advanced and chronic cases in this group, while most of those who received chemotherapy were early cases and more acute in nature. The Chinese prefer to take drugs rather than any type of surgery, and would even shun pneumoperitoneum if possible. An analysis of a group of patients treated with chemotherapy alone is under preparation and will be reported at a later date.

Discussion

A period of sanatorium rest and treatment is the ideal method of treating the tuberculosis patient. This is particularly important for the open and acute cases. Our program of ambulatory pneumoperitoneum as outlined above has helped many, but we feel and know that the solution lies in having sufficient sanatorium beds, where patients may receive adequate rest and care under medical supervision, free from economical worries and stresses.

There was no selection in our cases. Up to 1948, we only gave pneumoperitoneum where pneumothorax could not be successfully initiated and where we did not obtain an effective collapse after a reasonable period. Gradually we were surprised and convinced over the good results of pneumoperitoneum with minimal complications as compared with pneumothorax.

Since May 1952 we have prescribed chemotherapy whenever indicated and possible on our pneumoperitoneum cases. The number of inactive cases for six or more months having had chemotherapy and pneumoperitoneum is 179. This is approximately 50 per cent of all inactive cases (343) from pneumoperitoneum with and without chemotherapy. Chinese tolerate and do well with the addition of dihydrostreptomycin and isoniazid alone or in combination.

Since 1948 an increasing number of patients were given pneumoperitoneum and since 1953 it had supplanted pneumothorax entirely in our clinic.

CONCLUSION AND SUMMARY

(1) Ambulatory pneumoperitoneum was administered to 1031 Chinese between January 1941 and January 1954.

(2) Because of few complications in pneumoperitoneum, we discontinued pneumothorax in December 1952.

(3) The poor existing economical condition and lack of free sanatorium beds in China and Hong Kong encouraged the use of ambulatory pneumoperitoneum.

(4) Of the 1031 cases, 740 (71.8 per cent) were males, One hundred and fifteen (11.1 per cent) in the 15-20 years age group, 727 (70.5 per cent) in the 21-40, 139 (13.5 per cent) in the 41-50 and 50 (4.9 per cent) in the 51-70 years age group; 596 (57.8 per cent) were far advanced, 190 (18.4 per cent) moderately advanced and 245 (23.8 per cent) minimal cases.

(5) Nineteen had air embolism of whom two died. One had massive hemorrhage in the abdominal cavity. Eleven developed hernia and pneumoperitoneum had to be discontinued in 10. Abdominal effusions were successfully treated in eight with aspirations, diuretics and improved nutrition, two died from malnutrition and one failed to continue treatment.

(6) Six hundred and twenty four terminated treatment against medical advice of whom 15.2 per cent were moderately and 65.6 per cent were far advanced cases. Over 50 per cent of these had treatment for only one to three months, and the majority began treatment before 1948, when pneumoperitoneum was little known. Recently more and more early cases have been found who were willing to take this form of treatment and for longer periods. The results on those (126) who discontinued treatment under medical advice and those (281) carried on their treatment are encouraging. Among the entire 1031, there were only 303 (29.4 per cent) with no imimprovement, 116 (11.3 per cent) improved symptomatically, 269 (26 per cent) had symptomatic and film improvement. Three hundred and forty-three have been inactive for six months to four years.

(7) Since May 1952, isoniazid and dihydrostreptomycin, alone respectively, or in combination, and streptopas with or without isoniazid, were given one to 12 months to 312 patients receiving pneumoperitoneum. Most of these patients had early and acute disease, and cannot be satisfactorily compared with those who had no chemotherapy and whose lesions for the most part were more advanced and chronic. One hundred and seventy nine of the 312 pneumoperitoneum cases who had chemotherapy have been inactive for six or more months.

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CONCLUSION Y RESUMEN

1. Desde Enero de 1941 hasta Enero de 1954, se administró neumoperitoneo ambulatorio a 1031 chinos.

2. Con motivo de algunas complicaciones del neumoperitoneo, interrumpimos su uso en Diciembre de 1952.

3. Las malas condiciones enonómicas y la falta de camas gratuitas en Shina y en Hong Kong, nos animó a usar el neumoperitoneo ambulatoriamente.

4. De los 1031 enfermos, 740 (71.8 por ciento) eran hombres, 115 (11.1 por ciento) entre 15 y 20 años de edad, 727 (70.5 por ciento) entre 21 y 40 años, 139 (13.5 por ciento) entre 41 y 50 años y 50 (4.9 por ciento) de 51 a 70 años. 596 (57.8 por ciento) eran muy avanzados, 190 (18.4 por ciento) moderadamente avanzados y 245 (23.8 por ciento) mínimos.

5. Diecinueve sufrieron embolia gaseosa, de los que murieron dos. Uno tuvo hemorragia copiosa en la cavidad abdominal. Once presentaron hernia y el neumoperitoneo tuvo que interrumpirse en diez de ellos. Los derrames peritoneales fueron tratados con éxito en 8 casos con aspiraciones diuréticos y alimentación mejorada; uno murió de desnutrición y uno no continuó el tratamiento.

6. Seiscientos veinticuatro interrumpieron el tratamiento contrariando la opinión médica, de los que 15.2 por ciento eran moderados y 65.6 por ciento muy avanzados. Más del 50 por ciento de estos, tuvieron tratamiento por sólo uno a tres meses y la mayoría empezaron antes del año de 1948 cuando el neumoperitoneo era poco conocido.

Récientemente más y más tempranos casos se han encontrado dispuestos a seguir esta forma de tratamiento por períodos más largos. Los resultados en los que terminaron su tratamiento por consejo médico (126) y los que continuaron su tratamiento (281) son alentadores. Entre todos los 1.031 sólo hubo 303 (29.4 por ciento) que no mejoraron; 116 (11.3 por ciento) mejoraron sintomáticamente, 269 (26 por ciento) han tenido mejoría radiológica. Trescientos cuarenta y tres (33.3 por ciento) han permanecido inactivos desde seis meses hasta cuatro años.

7. Desde Mayo de 1952, la isoniacida y la dihidroestreptomicina una de ellas o ambas, y estrepto-PAS con o sin isoniacida, fueron dados de uno a 12 meses a 312 enfermos tratados también con neumoperitoneo. La mayoría de estos enfermos tenían enfermedad aguda y temprana y no pueden ser satisfactoriamente comparados con los que no tuvieron quimioterapia que fueron muy avanzados y crónicos.

Ciento setenta y nueve de los 321 que han tenido quimioterapia, son inactivos por seis o más meses.

RESUME

1. 1.031 Chinois ont été traités entre janvier 1941 et janvier 1954 par pneumopéritoine de façon ambulatoire.

2. Les auteurs ont abandonné le pneumothorax en décembre 1952, en tenant compte de la rareté des complications quand on utilise le pneumopéritoine.

3. Les mauvaises conditions économiques et le manque de lits de sanatorium disponibles en Chine et à Hong-Kong poussèrent à utiliser le pneumopéritoine ambulatoire.

4. Parmi les 1.031 cas, 740 (71,8%) étaient des hommes, 115 (11,1%) entraient dans le groupe des 15 à 20 ans, et 50 (4,9%) dans le groupe des 51 à 70 ans. 596 (57,8%) reprèsentaient des lésions très avancés, 190 (18,4%) des lésions modérément avancées, et 245 (23,8%) des cas minimes.

5. 19 firent une embolie gazeuse dont deux moururent. L'un eut une hémorragie massive dans la cavité abdominale. Onze eurent une hernie et le pneumopéritoine dû être cessé chez 10. Des épanchements abdominaux furent traités avec succès, chez 8 d'entre eux par des aspirations, des diurétiques et une amélioration de la nutrition. Deux moururent de dénutrition. Un cas fut un échec au traitement prolongé.

6. 634 cessèrent le traitement contre l'avis médical, parmi eux 15,2% avaient des lésions modérément ou très avancées (65,6%). Plus de 50% de ceux-ci ne furent traités que pendant un à trois mois; pour la plupart d'entre eux, le traitement fut commencé avant 1948, alors que le pneumopéritoine était peu connu. Ces temps derniers, les cas ont été découverts de plus en plus précocément et les malades désirent suivre cette forme de traitement pour de plus longues périodes. Les résultats de ceux (126) qui cessèrent le traitement après avis médical et de ceux (281) qui le poursuivent encore sont encourageants.

Parmi le groupe total des 1.031 malades, il y eut seulement 303 malades (29,4%) qui n'eurent aucune amélioration, 116 (11,3%) furent améliorés au point de vue symptomatique, 269 (26%) qui eurent des améliorations perceptibles sur les clichés. 343 (33,3%) ont été stabilisés pendant un temps d'observation de 6 mois à 4 ans.

7. Depuis mai 1952, l'isoniazide et la dihydrostreptomycine seules ou en association, et le "streptopas" associé ou non à l'isoniazide, furent donnés de 1 à 12 mois à 312 malades porteurs de pneumopéritoine. La plupart de ces malades avaient une atteinte précoce et aiguë et ne peuvent être comparés d'une manière satisfaisante à ceux qui n'eurent pas de chimiothérapie, et dont les lésions, pour la plupart étaient assez avancées ou chroniques. 179 malades parmi les 321 traités par pneumopéritoine en association avec la chimiothérapie sont restés stabilisés pendant six mois ou plus.

SCHLUSSFOLGERUNGEN UND ZUSAMMENFASSUNG

1. Ambulante Pneumoperitoneum-Behandlung-wurde angewandt bei 1031 Chinesen in der Zeit zwischen Januar 1941 und Januar 1954.

2. Wegen der wenigen Komplikationen beim Pneumoperitoneum setzten wir den Pneumothorax ab Dezember 1952 nicht länger fort.

3. Die schlechten wirtschaftlichen Existenzbedingungen und das Fehlen freier Heilstättenbetten in China und Hong Kong verstärkten den Gebrauch der ambulanten Pneumoperitoneum-Behandlung.

4. Von den 1031 Fällen waren 740 (71,8%) Männer, 115 (11,1% befanden sich in der Altersgruppe von 15 bis 20 Jahren, 727 (70,5%) in der Altersgruppe von 21—40, 139 (13,5%) in der Altersgruppe von 41—50 und 50 (4,9%) in der Altersgruppe von 51—70 Jahre; 596 Fälle (57,8%)

waren weit fortgeschritten, 190 (18,4%) mässig fortgeschritten und 245 (23,8%) waren minimale Fälle.

5. 19 Patienten erlitten eine Luftembolie, von denen 2 starben. Einer hatte eine massive Blutung in die Bauchhöhle. Bei 11 Kranken entwickelte sich eine Hernie, und das Pneumoperitoneum musste eingestellt werden bei 10. Abdominelle Ergüsse wurden in 8 Fällen erfolgreich mit Punktionen, Diureticis und verbesserter Ernährung behandelt, 2 starben an Unterernährung und einer unterliess es, die Behandlung fortzusetzen.

6. 624 beendeten die Behandlung gegen ärztlichen Rat, von denen 15,2% mässig und weit fortgeschritten waren (65,6%). Mehr als 50% von diesen hatten die Behandlung nur für 1—3 Monate bekommen, und bei der Mehrzahl begann die Behandlung vor dem Jahre 1948, als das Pneumoperitoneum noch wenig bekannt war. In der letzten Zeit fanden sich mehr und mehr leichte Fälle, die willens waren, diese Form der Behandlung für längere Zeitabschnitte durchzuführen. Die Ergebnisse von denjenigen (126), die die Behandlung mit ärztlichem Einverständnis beendeten, und denjenigen (281) die ihre Behandlung fortsetzten, sind ermutigend. Unter den ganzen 1031 fanden sich nur 303 (29,4%) ungebessert, 116 (11,3%) symptomatisch gebessert, 269 (26%) zeigten auf Röntgenfilmen Besserungen. 343 (33,3%) sind inaktiv geblieben in einem Zeitraum zwischen 6 Monaten und 4 Jahren.

7. Seit Mai 1952 wurde Isoniazid und Dihydrostreptomycin allein bzw. in Kombination und Strepto-PAS mit oder ohne Isoniacid für 1—12 Monate an 312 Kranke mit Pneumoperitoneum gegeben. Die meisten dieser Patienten hatten eine frühe und akute Krankheitsform und können nicht recht mit denjenigen verglichen werden, die keine Chemotherapie gehabt hatten und deren Herde grösstenteils weiter fortgeschritten und chronisch waren. 179 der 321 Pneumoperitoneumfälle, die mit Chemotherapie zusätzlich behandelt worden waren, sind 6 oder mehr Monate inaktiv geblieben.

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Case Report Section

Pulmonary Nocardiosis: Report of a Case Complicated by Tuberculosis*

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Although much attention has been given recently to fungus infections of the lung, relatively few cases of pulmonary nocardiosis have been described and in most of them the disease was in the terminal stages. The apparent rarity of the disease is largely due to failure to recognize the clinical manifestations and findings of nocardiosis. Moreover similarity between nocardiosis and pulmonary tuberculosis from a clinical and roentgenographic standpoint and the similar morphology of the causative organisms may lead to an erroneous diagnosis of tuberculosis in many cases of pulmonary nocardiosis. Even greater confusion may arise where both infections coexist. Recently we operated upon a patient with pulmonary nocardiosis and tuberculosis in whom the latter infection was not recognized prior to lobectomy. Specific antituberculosis therapy was instituted 14 days after operation and a dangerous spread of the tuberculosis process was controlled.

L. L., a 40 year old Latin-American male was admitted to Methodist Hospital on May 25, 1954 with a diagnosis of pulmonary nocardiosis. Symptoms began about nine months previously and consisted of fever, fatigue, and weight loss of 40 to 45 pounds. For the past 12 years he was employed by a sulphur producing company and was exposed to fine sulphur dust and sulphides. When he consulted his physician in November 1953, three weeks following the onset of cough and hemoptysis, sputum examinations revealed acid-fast organisms with mycelial branching suggestive of Nocardia asteroides. Tubercle bacilli were not isolated. Samples of sputum were used for guinea pig inoculation and the granulomatous lesion formed produced pure cultures of Nocardia asteroides (Figure 1).

Under his physician's care he received sulfadiazine approximately 6.0 grams daily until the present hospitalization. He became afebrile and the cough was relieved. Sputum examinations were negative for the first several weeks and then again became positive for Nocardia asteroides.

On admission to the hospital he appeared to be well nourished and in good, general condition. There were rales audible over the right upper lobe but no other significant abnormal finding was present.

Laboratory studies revealed normal hemogram and urinalysis showed a trace of protein and sugar. Serologic test for syphilis was positive. Sputum examinations revealed acid fast organisms which were presumed to be Nocardia asteroides and results of cultures were not available at the time of thoracotomy.

Roentgenograms of the chest revealed dense infiltration and consolidation of the right upper lobe which contained multiple cavities (Figure 2). The remainder of the right lung and the entire left lung were uninvolved.

On May 29, 1954, following negative bronchoscopy thoracotomy was performed under ether anesthesia. The pleural space was almost completely obliterated by the inflammatory process. After the adhesions were divided, the lung was carefully palpated. The upper lobe was totally atelectatic and consolidated and the bronchopulmonary nodes were enlarged. Upper lobectomy was done and two nodules were removed from the middle lobe by wedge resection. The lower lobe was completely free of disease.

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After operation he continued on sulfadiazine and blood sulfa level was maintained between 3.6 and 7.2 mgm per cent. In addition he received penicillin and terramycin injections and remained afebrile. Because of a persistent air leak from the thoracotomy tube right phrenic crush was done on the ninth day after operation and the pulmonary leak healed promptly. He remained afebrile and his appetite improved.

On the 14th day after thoracotomy bilateral parenchymal infiltration was noted in roentgenograms of the chest (Figure 3). Sputum was then reported to be strongly positive for M. tuberculosis and cultures of sputum made before operation revealed colonies of the same organism. Fortunately he remained surprisingly well. Streptomycin and para-aminosalicylic acid was begun and continued during the remainder of the hospital stay. He improved steadily and was discharged from the hospital June 17, 1954.

Since discharge he has remained well. Streptomycin and para-aminosalicylic acid were continued for six months. The latest roentgenogram of the the chest revealed resolution of the bilateral pneumonic process and sputum examinations are negative for Nocardia asteroides and Mycobacterium tuberculosis.

Pathologic examination of the specimen of the right upper lobe revealed an abscess cavity measuring 3.5 cm. in diameter with the remainder of the lobe atelectatic and infiltrated with a grayish tan necrotic tissue (Figure 4). Microscopic examination of the lung revealed a well-defined granulomatous reaction with tubercles and caseation necrosis. Within occasional Langhans' giant cells and elsewhere were seen elongated bacilliform structures. Acid fast stains of the lymph nodes disclosed irregularly staining acid-fast organisms with inconstant morphology and a tendency to branching.

Discussion

The first known case of a human infection by a fungus known as Cladothrix asteroides was reported in 1891 by Eppinger[9] who described a patient dying of brain abscess from which an aerobic gram-positive, acid-fast actinomyces was identified. In 1888 Nocard[17] had reported an acid-fast sporothrix isolated from cows thought to have tuberculosis. The organism in both instances was subsequently proved to be identical and became known as Nocardia asteroides. Isolated cases of pulmonary nocardiosis appeared during the ensuing years and in 1921 Henrici and

FIGURE 1

FIGURE 2

Figure 1: Photograph of culture made of sputum at onset of illness showing typical wrinkled and granular colony of Nocardia asteroides.—*Figure 2:* Roentgenogram of chest made just prior to operation showing infiltration and cavitation in right upper lobe.

Gardner[13] made the first extensive review of the medical literature collecting 26 established cases of nocardiosis, 23 of which were pulmonary, and added another. Since their collected review occasional isolated reports have appeared bringing the total reported cases of pulmonary involvement to 46.[2]

Nocardia asteroides is an aerobic, gram-positive, acid-fast organism which grows readily on a variety of simple media, the colonies appearing wrinkled and granular (Figure 1). Pigmentation may vary from yellow to an orange red. Culturally and morphologically the organism is closely related to Mycobacterium tuberculosis. Tubercle bacilli vary in length from one to four μ, whereas the organism, N. asteroides, is one μ, or less in length and shows a distinct tendency to branching.[1,8]

Nocardia asteroides produces a granulomatous lesion usually containing an exudate in which pink or black granules are demonstrated microscopically. The organism is pathogenic for laboratory animals which frequently die from the toxic effect of inoculated material rather than from extensive invasion of the fungus.[1,8] In man nocardiosis is usually contacted by air-borne contamination but may be introduced by trauma and small cutaneous puncture wounds. There have been no reported instance of transfer of disease from man to man or animal to man.[8, 16]

Symptoms of nocardiosis are usually respiratory including chronic productive cough and occasional hemoptysis. Complaints of malaise, chills, fever, anorexia, weight loss, and night sweats are common. Symptoms of headache, nausea and vomiting may indicate the presence of cerebral involvement a not infrequent complication of the disease according to

FIGURE 3

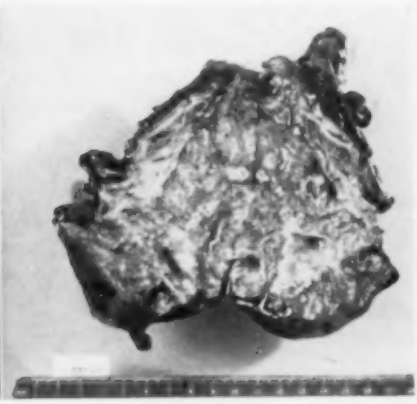

FIGURE 4

Figure 3: Roentgenogram of chest made 14 days after operation showing pleural thickening on the right and fresh bronchopneumonic infiltration of the left lung.—*Figure 4:* Photograph of specimen of right upper lobe showing atelectasis, consolidation, and cavitation.

some.[14, 15, 19] Metastatic lesions may occur as a result of hematogenous spread.[8]

Roentgenologically, an infiltrative process of the lungs is manifested which may lead to multiple cavitations. Drake and Henrici in 1943, showed in animals there was no cross reaction between Nocardia antigen and tuberculin.

With early diagnosis and institution of proper therapy the prognosis is favorable. However, in the event of pyemia and metastases the disease is probably fatal.[21] Benbow, Smith and Grimson[2] reported two cases of nocardiosis with pulmonary and subcutaneous involvement that were considered cured. These patients received bed rest, surgical drainage, vitamins, sulfonamides, iodides, and x-ray. Since then an increasing incidence of cures is noted.[23] Most patients showing favorable results received sulfonamides, however, Hague and associates[12] in 1949 reported a case of pulmonary nocardiosis in a 64 year old female in which penicillin, streptomycin, and aureomycin, but not sulfonamides, inhibited the organism.

In our patient diagnosis of pulmonary nocardiosis was firmly established prior to operation and the systemic manifestations of the disease were adequately controlled by sulfadiazine. Although tuberculosis was suspected from the time of initial examination, identification of the tubercle bacillus was not possible. It may be that subsequent control of the fungus infection by sulfonamide permitted an emergence of the tuberculous process which flourished in an uncontrolled manner. Thus, after operation a dangerous spread of the tuberculous infection occurred while fungus disease remained under control with sulfadiazine. A possible fatal outcome was averted by final recognition of fulminating pulmonary tuberculosis and institution of appropriate therapy. To our knowledge no previous case of coexisting pulmonary nocardiosis and tuberculosis has been reported. Fortunately the patient made a complete recovery under treatment for both diseases.

References will appear in reprints.

Agenesis of the Lung

Case Report With Five Year Follow-Up

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Jackson, Mississippi

Agenesis of the lung is a congenital absence or hypoplasia of one or both lungs. This is not a common condition. As of January 1, 1954 there were less than 150 cases reported in the medical literature.[1] Most of these were discovered at autopsy.

In 1950 Ingram[2] reported that only 18 cases had been diagnosed during life up to that time.

In 1953 Oyamada, Gasul and Holinger[3] reviewed the literature to date listing 73 cases of agenesis, 38 cases of hypoplasia, 4 cases of newborn infants with congenital absence of both lungs and 21 cases with agenesis or congenital hypoplasia of the lung but with the description being incomplete or the diagnosis not being definitely established.

Schneider[4] has described three types of pulmonary agenesis depending on the development of the bronchus and lung tissue: (1) One lung is absent without any development of the lung or bronchus, (2) there is complete absence of lung tissue but there is a poorly developed bronchus on the involved side and (3) the bronchus is small, poorly developed and connected to a mass of rudimentary lung tissue.

The etiology of this faulty lung development is unknown. The condition is often associated with other anomalies of the tracheobronchial tree and even other parts of the body. Cases coming to autopsy have uniformly shown emphysema of the remaining lung, malformation of the cartilagenous skeleton of the trachea such as extra cartilagenous rings or narrowing of trachea and absence or malformation of pulmonary vessels.[5] Hypertrophy of the right heart has not been noted. There is little difference in incidence between the right and left side. About 14 per cent of the cases are stillborn or die within the first few weeks of life.[6]

Symptoms: The patient may be completely asymptomatic. He may have mild respiratory distress on exertion. A few cases have dyspnea, cyanosis, recurrent choking spells, wheezing, stridor and hemoptysis on occasions. The amount of respiratory distress is dependent upon the condition of the remaining lung and the associated congenital anomalies. Respiratory infections are common. The infant is susceptible to attacks of bronchopneumonia and later the child is susceptible to frequent colds and dyspnea on exertion.

Diagnosis: The condition can usually be distinguished from atelectasis of the newborn by absence of respiratory distress. The chest is usually symmetrical in the infant but as the child grows older there may be slight asymmetry. There is mediastinal shift to the involved side. The

remaining lung may extend past the midline. Bronchoscopy reveals the absence or deformity of bronchi to the effected side. Bronchograms confirm this deformity. Angiocardiograms reveal absence or rudimentary blood supply to the involved side.[2, 7]

Prognosis: The prognosis in any case is influenced more by the associated anomalies than by the agenesis of one lung. Many die in infancy but some live a normal life span. Twenty-three persons (27 per cent) of the series reviewed by Hochberg and Naclerio were known to have lived to be between 15 and 72 years of age.

The involvement of the only existing lung by severe infection, foreign body or trauma may prove fatal at any time.[7, 8] Due to the fact that there may be unknown associated congenital anomalies these individuals are not always good surgical risks. This should be borne in mind when submitting them to elective surgery.

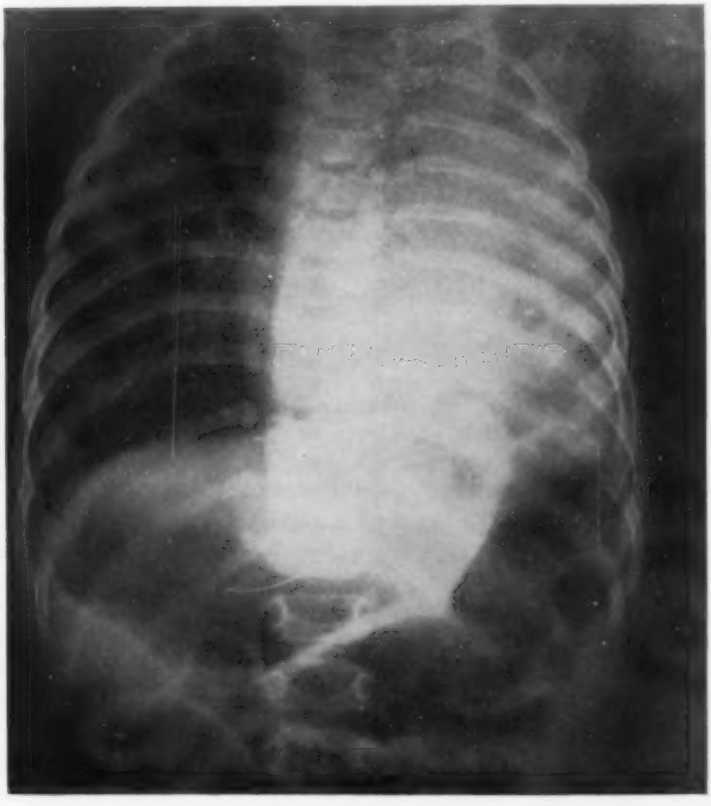

FIGURE 1: X-ray film of chest May 25, 1951. Mediastinal structures on right. Symmetrical chest.

Case Report

E. I. K. white, girl, age 6½ months, was first admitted to the Mississippi Baptist Hospital on May 25, 1951. The mother stated that she was an 8 month baby, weighing 5 lbs. 11 oz. at birth. She was fed from birth by formula and ate well. She was never cyanotic and only slight dyspnea was noted on exertion at any time. This was not marked. She did not seem unusual except in failure to gain weight as rapidly as the average child. About three weeks before admission, she developed what was thought to be a cold. Dr. Swink Hicks of Natchez, Mississippi, was consulted and referred her for further examination.

This revealed an alert, apparently healthy, well nourished white girl, weighing 12 lbs. The chest was symmetrical but there was impaired resonance to flatness over the right hemithorax. There was no cardiac dullness on the left. Heart sounds were best heard on the right. Breath sounds were absent over the right hemithorax. X-ray films made before admission with barium swallow revealed no evidence of diaphragmatic

FIGURE 2: Photograph of patient, age 5 years, with agenesis of right lung. Note slight asymmetry of the chest with prominence of right supraclavicular and infraclavicular fossae. The right shoulder is lower than left.

hernia. The stomach and intestine were in normal position. Roentgenogram of chest, Fig. 1, taken May 26, 1951, revealed homogenous density in right hemithorax with shift of mediastinal structures to that side. The left lung was clear. The chest cage appeared symmetrical. The intercostal spaces were found to be equal on the two sides.

A blood examination revealed a red blood cell count of 13 grams, white blood cell count 10,100 with 63 per cent lymphocytes, 16 per cent segments, 15 per cent monocytes and 6 per cent eosinophils.

On May 26, a 3½ mm. bronchoscope was passed. The trachea was deviated to the right and it appeared to be of normal size. The carina was much wider than normal and was a little red. The right main stem bronchus took off at more of an angle than usual and ended abruptly at about 1 cm. beyond the bifurcation of the trachea. At the end it appeared to be covered with normal mucous membrane. There was no evidence of intraluminal tumor or foreign body. The blind bronchial stump was probed gently with a suction tip. An unsuccessful attempt was made to obtain a biopsy. She did well after this examination did not develop evidence of laryngeal obstructions and was discharged about 36 hours later.

A diagnosis of agenesis of the right lung was made. Bronchography and angiocardiography did not appear justified at the time.

During the last five years her general health has remained good except for frequent colds. She has not gained weight as rapidly as the average child. When last examined in February, 1956, she weighed 32¼ lbs. and her height was 45 inches. There was

FIGURE 3: X-ray film of chest November 18, 1955. Mediastinal structures in right hemithorax, some narrowing of intercostal spaces on right and right shoulder dropped.

slight asymmetry of her chest, Fig. 2. The right shoulder is carried at a lower level than the left.

X-ray film of chest on November 18, 1955, Fig. 3, revealed normal appearing left lung with mediastinal structures shifted to the right. There is slight narrowing of the intercostal spaces on the right.

She is extremely active and does not experience dyspnea even on extreme exertion. We have not been able to detect other congenital anomalies. Apparently her prognosis is good.

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On Clear Bordered Images of the Left Apex

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In pulmonary tuberculosis, the study of morphology and topography of lesions with the help of radiology requires a perfect knowledge of the images encountered. Tomography plays a capital role in the search for lesions.

This role is particularly important for the study of the extreme pulmonary apex for the region is difficult to analyze even on the best ordinary roentgenograms because of overlying bone shadows.

The aim of our communication is to show the difficulties encountered in defining certain clear bordered images of the left apex and the problems created by these images.

For instance, here is the case of Mr. B, state employee, aged 35, who presented fibrous tuberculosis of the upper part of both lungs (Fig. 1). First extrapleural pneumothorax is instituted on the right side (Fig. 2). Then, we hesitated about what to do for the left side where a clear bordered image is revealed by tomographic exposures at 9, 10, 11 centimeters of the back plane. We were unable to visualize a draining bronchus of the eventual cavity. The patient's general condition improved after pneumothorax and the sputum was negative, so the left side was untreated.

The patient asked for reemployment but, owing to the lesion of the left apex the medical committee refused to accept him, stating that the image indicated a tuberculous cavity.

We then made a series of tomographic exposures of the left apex by the magnifying method previously described. At 11 centimeters our bordered image is seen in a particularly clear manner (Fig. 3). A cavity with sclerous wall and with an internal epithelium layer seemed possible.

About this time we had the opportunity to examine Mr. H., 25 years old who presented a cavity in the left lung (Fig. 4) and left extrapleural pneumothorax was done (Fig. 5). We were surprised to find on the tomographic exposures that we had the same clear image as the one observed in the previous case (Fig. 6).

So, the interpretation of a left apex cavity which was valuable for Mr. B., was not valuable for Mr. H., because in the last case there was no lung nor pleura in the upper part of the left thorax owing to the pneumothorax.

So what is this bordered image which is the same in a left apex with pleura and lung and in another left apex without pleura and lung? We can only speak of a parietal mold constituted by anatomic formations.

But what anatomic formations?

Angiography and thoracic endoscopy which could have helped were refused by the patients. Among the explanations for this image . . . such as a particular disposition of the apex ligaments, a particular disposition of

From the Centre Medical M.G.E.N.

FIGURE 1

FIGURE 2

FIGURE 3

FIGURE 4

FIGURE 5

FIGURE 6

the subclavian vessels, or of the thoracic duct . . . the best seems to be the abnormal situation of the left azygos vein.

One of us with le Bourdelles in 1932 showed the left azygos lobe is a reality. This had been noted anatomically for the first time by Wrisberg in 1778, then by Bostrom and by Merkel. In the case described by Wrisberg the left azygos vein was situated before the costo-vertebral articulations where it received the intercostal veins from the 10th to the third spaces. Then it made a curve towards the subclavian vein, its way being around the external upper part of the left lung and entering gently into the parenchyma, the left apex seemed a small hernia.

It is then easy to imagine that if the lung tissue is pulled down as occurs during the creation of extrapleural pneumothorax, a vasculo-conjunctive mold remains which may represent the image that we noticed in Mr. H's case. Also, the subclavian vessels are often seen as ribbon-like images on tomographic exposures at 11 centimeters of the back plane which supports our explanation.

Sometimes, on the right side, similar images are made in evidence and seem particularly demonstrable when an azygos lobe is present.

What ever the explanation, we believe the image is important and should not be mistaken for cavitation.

Disappearance of Tuberculosis in Patient Treated with Anti-tuberculosis Drugs for Pulmonary Tuberculosis Co-existing with Bronchogenic Carcinoma*

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The present case is being reported as an example of pulmonary tuberculosis which was unequivocally established clinically and yet could not be found pathologically in a patient who died with co-existent bronchogenic carcinoma after receiving anti-tuberculous chemotherapy. Similar findings have been published by Kumar.[1]

J. P., a 53 year old Negro porter, was referred to the Bedford Chest Clinic on November 18, 1953, for cough and expectoration of two weeks duration. He had temperature 99° F., pulse 80, respiration 20, weight 169½. The only abnormal findings were in the lungs where dullness and occasional moist rales were heard over the lower two-thirds of the right lung posteriorly and over the lower one-third, anteriorly. A chest roentgenogram on November 18, 1953, (See Figure 1) disclosed a disease process in the right lower lobe. He reacted to the Mantoux Test 1:1000 to a one plus degree. A definite diagnosis was not made at first and he remained under the

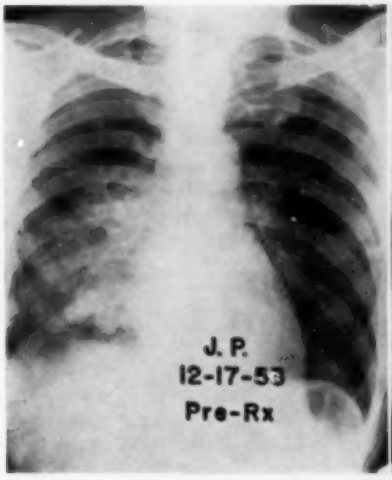

FIGURE 1

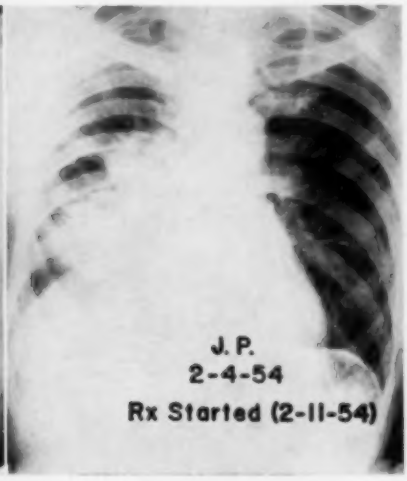

FIGURE 2

Figure 1: Pneumonic infiltration right lower lobe with many cavities.—*Figure 2:* Film immediately prior to onset of antituberculous chemotherapy; no change from December 17, 1953.

*From the Bedford Chest Clinic, New York City Bureau of Tuberculosis, Department of Health.

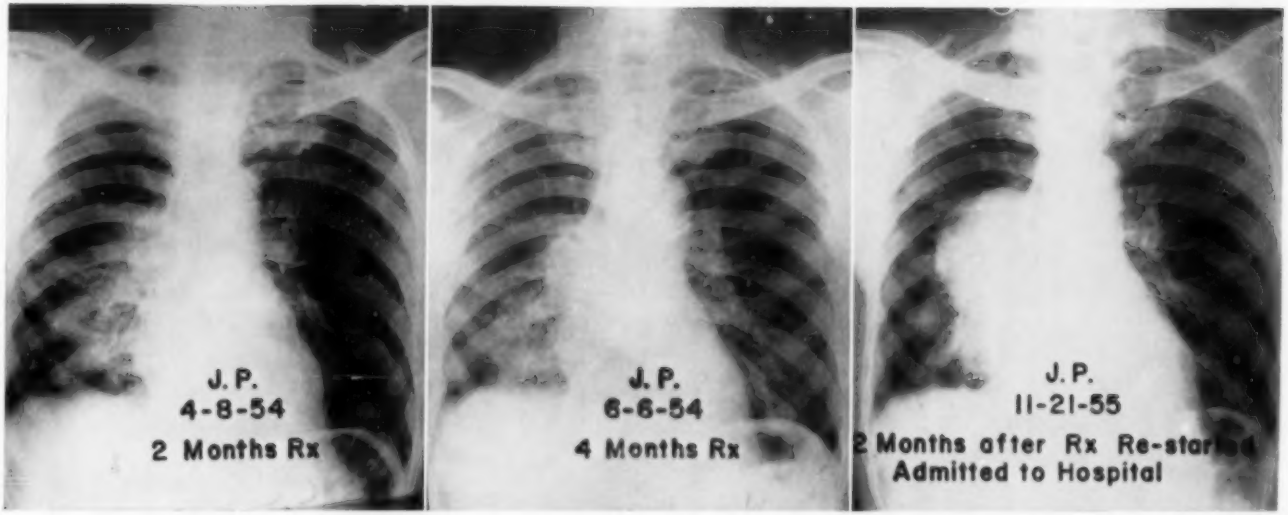

FIGURE 3 FIGURE 4 FIGURE 5

Figure 3: Considerable resolution right lower lobe.—*Figure 4:* Further resolution of infiltration at right base; no cavity visible; small density noted adjacent to right hilum.—*Figure 5:* Film shows mass situated in apex of right lower lobe.

supervision of his private physician who prescribed anti-microbial drugs (type not determined) without benefit. He persistently refused hospitalization. It was not until February, 1954 (See Figure 2) that he returned to the clinic for further care.

Because of no response to previous treatment, chemotherapy consisting of 300 mgs. isoniazid and 12 gms. of PAS was started February 11, 1954, prior to bacteriological confirmation of the suspected tuberculosis. Two pre-treatment sputum cultures were reported positive and another taken April 13, 1954 was also reported positive. By June 9, 1954 (See Figures 3 and 4) marked improvement was present both roentgenographically and symptomatically. After the last clinic visit on June 6, 1954, he continued to take treatment to August 1, 1954. On the latter date, he suddenly left for North Carolina to stay with some relatives and remained there without medical supervision or treatment until July 1, 1955, when he returned to New York City. He did not report to Bedford Chest Clinic until October 17, 1955, (See Figure 5). At that time he had relatively few complaints and no significant positive physical findings. However, a roentgenogram taken at this time showed a striking increase in the hilar density first noted on June 6, 1954. He was promptly placed on isoniazid and streptomycin (1 gm. twice weekly) and finally persuaded to enter the Brooklyn Jewish Hospital on December 6, 1955, where the two drugs were continued. Six laryngeal and five sputum cultures were negative at the clinic between May 8, 1954, and December 7, 1955. At the hospital bronchoscopic examination was non-contributory, and scalene biopsy was negative. Papanicolaou smears were negative, and electrocardiogram studies showed an old myocardial infarction. Because of the undiagnosed hilar mass, thoracotomy was performed and a large resectable tumor was found in the right lower lobe. While the tumor was being resected, he developed cardiac arrest and died.

The autopsy performed by Dr. David Grayzel, pathologist at the Jewish Hospital, Brooklyn, revealed an oat cell bronchogenic carcinoma of the right lower lobe; the hilar nodes were free from cancer. The vessels were congested. The tumoral masses were composed of nests and sheets of atypical cells. Perl formation was noted in places. The interstitial tissues between the sheets were infiltrated with chronic and acute inflammatory cells. No evidence, gross or microscopic, of pulmonary tuberculosis was found, in spite of painstaking examination of all the organs for histologic or bacteriologic evidence of this disease.

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Surgical Treatment of Coarctation of the Aorta

Report of the Section on Cardiovascular Surgery*

In 1945 Crafoord and Nylin[1] and Gross and Hufnagel[2] independently reported the feasibility of surgical correction of coarctation of the aorta. Since that time a significantly large number of surgically treated cases have been reported in the medical literature, thus providing valuable information regarding the indications for surgery, the associated morbidity and mortality and the results obtained. However, since the total experience is limited to a developmental period of just over a decade and since, in all probability, the majority of surgically treated cases have not been reported, the answers to many pertinent questions regarding this therapy are still forthcoming. Sufficient statistical information is available to indicate that the prognosis of patients with coarctation without surgical correction is poor. The average duration of life in a group of 200 patients collected by Abbott[3] and reported in 1928 was 32 years. In an additional group of 104 collected cases reported in 1947 by Reifenstein, Levine and Gross[4] it was found to be 30.5 years. As judged by Brown[5] only one-tenth of the patients having coarctation of the aorta live past the age of 50 years. The need for a method to improve upon this rather dismal outlook is obvious. Therefore, if the risks involved in surgery prove statistically to be relatively small and the late results favorable, as experience to date would seem to indicate, then there should be no hesitancy on the part of the family physician in recommending surgical treatment. The purpose of this report of the Section on Cardiovascular Surgery of The American College of Chest Physicians is 1) to attempt to evaluate the results to date and thus clarify the indications for operation, and 2) to bring forth any information based on past experience that may be of help in avoiding difficulties and improving the results obtained. The report is based on an analysis of 1601 cases treated surgically by 36 of the members of the Surgical Advisory Committee of The American College of Chest Physicians who are outstanding cardiovascular surgeons from representative areas throughout the world (See below). Since some of the participating surgeons did not answer all of the questions included in the questionnaires, the number of cases included in studying various specific problems, of necessity, must vary. Even so, the numbers are large enough to indicate trends which undoubtedly will be helpful in solving some of the problems with which we are faced.

Nature of the Lesion and Associated Defects

In 1133 cases 73 were classified as being preductal or "infantile" and 1060 postductal or "adult" in type. Some surgeons with extensive experience did not feel inclined to make subdivision because there is so much overlapping between the two types, particularly when a patent ductus arteriosus is present.

*Presented at the 22nd Annual Meeting, American College of Chest Physicians, Chicago, Illinois.

Important associated defects were present in 431 (36.6 per cent) of the 1187 cases where a careful study was made. The various lesions and their frequency are given in Table I.

Patency of the ductus arteriosus was most common, being present in 189 (15.9 per cent) of cases and fortunately is a correctable defect.

Deformity of the aortic valve was second in frequency, being present in 130 (11.7 per cent) of cases. Aortic insufficiency was present in 103 and stenosis in 27 instances. While the actual extent of these two components is difficult to assess with accuracy, most surgeons accept cases for surgical treatment if the valvular involvement is not serious and a few feel that operation should be done even in the presence of major degrees of involvement. Concomitant aortic valvulotomy and/or the insertion of a Hufnagel valve has been done in many of these patients. This practice to date apparently has been rare.

Specific criteria were not given to indicate when simple dilatation of intercostal arteries or the aorta distal to the point of obstruction became "aneurysmal." However, a significant degree of dilatation of these structures was relatively common. The marked dilatation of the thin-walled intercostals was of practical importance since it was the cause of serious or fatal hemorrhage in a number of instances. The incidence of serious associated defects both correctable and uncorrectable varied considerably in the different groups reported, indicating that some surgeons were much more strict with respect to indications for surgery, with resultant differences in mortality rates. The presence or absence of serious uncorrectable

TABLE I
ASSOCIATED DEFECTS, 1187 CASES OF COARCTATION OF THE AORTA

	Number	Per Cent
Patent ductus arteriosus	189	15.9
Aortic valve deformity with insufficiency	103	8.6
Aortic valve deformity with stenosis	27	2.2
"Aneurysm" intercostal artery	40	3.3
"Aneurysm" post-coarctation	24	2.0
Interventricular septal defect	22	1.8
Subacute bacterial endocarditis preop.	13	1.0
Subacute bacterial endocarditis postop.	6	0.5
Mitral valve deformity with insufficiency	3	0.2
Mitral valve deformity with "atresia"	1	
Pulmonary stenosis	1	
Interatrial septal defect	1	
Subendocardial fibroelastosis	1	
TOTAL	431	36.3

associated defects should be considered when the risks of surgery are being discussed with individual patients.

Location and Extent of Coarctation

Although the question was not asked specifically, coarctation at unusual levels and narrowing over unusually long distances must have occurred infrequently. This seems to be indicated by the fact that unusual locations were mentioned in only five instances and in these inability to correct the lesion was not reflected in the causes of death or poor results. Extensive narrowings must have been uncommon since grafts were used in only 56 of 1405 cases and in many of these direct suture almost certainly could have been done if the surgeon had not inclined to use grafts frequently as a matter of personal preference. To illustrate this point, one surgeon used homografts in 15 of his total of 22 cases, all of which were classified as being postductal in type.

Angiocardiography and Retrograde Aortography

In the group of 1165 cases where the employment of these diagnostic procedures was reported, angiocardiography was used on 268 occasions and retrograde aortography on 136. The occurrence of serious or fatal reactions was not reported.

Wide divergence of opinion regarding the need for these diagnostic procedures obviously exists, since some surgeons use them more or less routinely while others, including some with the greatest experience, use them rarely or not at all. In view of the risk involved, particularly in infants, and the rarity of coarctation of unusual location or extent, it would seem reasonable that these studies should be reserved solely for patients presenting signs or symptoms that suggest the presence of atypical lesions or serious associated defects which might alter significantly the plan of surgical attack. This would seem particularly true if homografts or plastic grafts were readily available in the event that an unusually long coarctation were encountered.

Indications for Surgery

The indications for surgery were given in a total of 1223 cases (Table II).

In some instances both hypertension and congestive failure were major indications in the same patient. Thirty-one surgeons expressed their current feelings regarding the indications for surgical correction of coarctation of

TABLE II

INDICATIONS FOR OPERATION 1,223 CASES—COARCTATION

	Number of Cases	Per Cent
Hypertension	1,055	86.2
Congestive failure	119	9.7
Presence of lesion	77	6.2
Other	42	3.4

the aorta in various ways. Sixteen feel that all cases should be treated surgically unless definite contraindications exist. Fifteen feel that in children below an age averaging six years and in adults over an age averaging 32 years, surgery should be done only if outspoken hypertension, cardiomegaly, heart failure or other serious related conditions are present. Only three surgeons specified an upper age limit as a contraindication and this age averaged 34 years.

Mortality Rates

The gross operative mortality rate—up to three months after surgery—in 1601 cases was 8.6 per cent. As expected, the mortality rate was higher in the younger and older age groups (Table III).

In general higher mortality rates were encountered in the groups in which a greater percentage of young or old patients was accepted for treatment and also in the groups in which a greater percentage of serious uncorrectable associated defects was included. However, several surgeons obtained unusually low operative mortality rates in spite of the fact that a high percentage of patients under one year of age and/or a similar high percentage of patients in the older age group was included. This suggests immediately the probability that many of these patients were operated upon without unnecessary delay before their general condition had deteriorated to such a degree that a high operative mortality rate was unavoidable. The experience of Mustard, et al,[6] seems to support this statement. In managing 90 infants and children with coarctation of the aorta, they found that those who present signs or symptoms of the condition in infancy constitute two-thirds of all individuals with coarctation, and since few of them will survive the first year of life without surgery, removal of the obstruction should be carried out without delay whenever possible. They point out that in children under one year of age with preductal lesions, the mortality rate is highest and that even a few days' delay in instituting treatment may result in a fatal outcome.

With reference to the older patients, if surgery is deferred sufficiently long, such irreversible complications as aneurysm of the aorta, intercostal or cerebral arteries, myocardial insufficiency, renal impairment, etc., may

TABLE III

OPERATIVE MORTALITY RATES ACCORDING TO AGE
1,601 CASES—COARCTATION

Age - Years	Number of Cases	Number of Deaths	Per Cent
0 - 3	130	21	16.1
4 - 15	616	42	6.8
16 - 30	653	52	7.9
Over 30	202	23	11.3
TOTAL	1,601	138	8.6

well keep the operative mortality rate at an unnecessarily high level and the improvement rate low.

In 1133 cases where the type of coarctation was specified 1060 were of the postductal or adult type with an operative mortality rate of 7.8 per cent and 73 of the preductal or infantile type with a rate of 28.7 per cent.

Causes of Death

The causes of death in the postoperative and late periods in 1536 cases are given in Table IV.

Cardiac Conditions

Cardiac conditions of various types are by all odds the most frequent cause of death, being responsible for the fatal outcome in 51 (37.7 per cent) of the total of 135 deaths. The following are included in this category: cardiac failure, including that due to uncorrectable lesions, pulmonary edema, shock, cardiac arrest and ventricular fibrillation. This seems to indicate the extreme importance of careful preoperative preparation and avoidance of anoxia, acute hemorrhage and all other controllable factors which tend to cause or aggravate these serious conditions. Again, the appli-

TABLE IV

CAUSES OF DEATH FOLLOWING SURGERY, 1,536 CASES OF COARCTATION

	Postoperative To 3 Months	Late	Total
Heart failure—pulmonary edema—shock	30	3	33
Disruption of anastomosis (or graft-1)	28	0	28
Cardiac arrest or fibrillation	18	0	18
Hemmorhage-operative	16	0	16
Cerebrovascular accident	4	1	5
Necrotizing arteritis	5	0	5
Embolism	3	0	3
Septicemia	3	0	3
Empyema	3	0	3
Atelectasis	3	0	3
"Medullary ischemia"	2	0	2
Coronary thrombosis	2	0	2
Rupture of aneurysm	0	2	2
Necrosis and thrombosis of anastomosis	1	0	1
Gastroenteritis	1	0	1
Drowning	0	1	1
Suicide	0	1	1
Unspecified	6	2	8
TOTAL	125	10	135

cation of surgery before irreversible changes have developed should prevent at least part of these fatalities. Late deaths after the three month postoperative period occurred in only eight cases from causes most of which are not related to the surgical procedure.

Disruption of the Anastomosis

This complication was the next most common cause of death, accounting for 28 (22.4 per cent) of the 125 postoperative fatalities. Because of this an attempt was made to determine the factors which might be responsible for this generally fatal complication. Although the incidence of probable or proved infection at the operative site was not asked for specifically, still the reporting surgeons indicated that such was present in 11 of the 28 fatal disruptions. Four additional cases were associated with postoperative subacute bacterial endarteritis but the relationship between the two complications was not specified. The frequency of this type of infection as well as three cases of septicemia and two of empyema, all of which terminated fatally, probably can be explained on the basis of gross airborne contamination due to the long wound exposure time. Measures to minimize this as well as more intensive prophylactic chemotherapy in the early postoperative period may well help to control these serious complications.

The technique used in the anastomosis might have a bearing on the incidence of disruption. In 918 cases where sufficient details were given to allow evaluation, an everting mattress suture technique was employed on 650 occasions with disruption in 17 (2.6 per cent). A simple continuous non-everting suture technique was used on 268 occasions with disruption in three (1.1 per cent). The higher incidence of disruption in the mattress suture group most probably is due to imperfect technique with placement of the sutures at varying distances from the cut ends of the aorta and tied with varying degrees of tension. Thus, if the tension happens to be excessive on the sutures farthest from the aortic ends they will tend to cut through the wall as a result of pressure necrosis, thus producing a transverse laceration which is apt to remain open because of the longitudinal pull of the aortic ends. On one occasion severe hemorrhage occurred from this cause at operation, but repair was possible. After one such suture cuts through, excessive tension will then fall on the adjacent sutures, thus tending to set up a vicious circle which may terminate in complete disruption. This, of course, is more apt to occur if interrupted sutures are used. When the simple non-everting continuous technique is used, equalization of tension on the individual stitches occurs readily. Even if the simple interrupted technique is employed the laceration produced as a result of pressure necrosis will be linear rather than transverse and therefore progressive healing is apt to take place. The linear laceration will stop as soon as the tension on the individual sutures becomes equalized. These considerations suggest that the mattress suture technique, particularly if it is interrupted, should be avoided unless the surgeon is an unusually capable technician. The effect of continuous suture techniques in preventing growth of the anastomosis has not been settled, but reports to date seem to indicate that this probably

will prove to be of less significance than has been anticipated. In 1405 cases grafts were utilized in 56 instances, all arterial homografts with the exception of one synthetic plastic. Disruption occurred three times (5.3 per cent) and in no instance was the presence of infection mentioned. In 1349 cases in which grafts were not used, disruption occurred 24 times (1.7 per cent). These figures would suggest that the use of grafts may prove to be associated with a much higher incidence of disruption than direct suture of the arterial ends.

Hemorrhage

Hemorrhage during surgery was the cause of death in 16 cases (12.8 per cent), usually from laceration of the extremely thin-walled, friable and markedly dilated intercostal arteries. This complication undoubtedly can be minimized by operating at an earlier age before excessive dilatation and thinning occurs and by meticulous care to avoid trauma, especially that caused by a shearing force applied during ligation of these vessels. The fact that 35.2 per cent of all postoperative fatalities were due to hemorrhage at the time of surgery or to disruption of the suture line, emphasizes that the surgical repair of coarctation of the aorta is associated with certain technical problems which are unique to this procedure alone and which can be mastered only by unusually good surgical technique plus actual clinical experience. The importance of this concept is emphasized by the experience of Gross[7] who reported 15 fatalities in his first 100 cases and only two in his next 100. Also, Clagett and Jampolis[8] reported a mortality rate of 7.1 per cent in 70 cases followed by 55 in which there was no mortality. Therefore, if we hope to avoid unnecessary serious complications or fatalities the total number of surgeons who operate upon these cases should be kept as small as is reasonable and practical and the quality of their technical ability as high as possible. The advisability of such limitation seems justified not only on theoretical grounds but also from a practical standpoint since most of the 36 surgeons participating in this survey reported relatively small groups of cases. Only two surgeons reported over 100 cases and these came from large clinics. Two-thirds of the surgeons reported series of 50 cases or less and one-third of them 25 or less. When one considers that these procedures have been used over a considerable period of time (from 1945 up to the present time), it is easy to appreciate that improvement from repetition in many instances must have been negligible just as it must continue to be if this relatively infrequent condition is cared for by too many surgeons.

Results of Surgery

The state of health of the survivors was evaluated with reference to the degree of relief of hypertension and also with reference to his general postoperative condition. The effect of the operation on blood pressure readings was reported in 1230 patients (Table V).

Normal blood pressure readings were present in 72.0 per cent of the survivors. The blood pressure was reduced, but not to a normal level, in 23.2 per cent. Hypertension persisted in only 4.7 per cent of the entire group.

TABLE V
EFFECT ON HYPERTENSION, 1,230 SURVIVORS—
SURGERY FOR COARCTATION

Age - Years		0 - 3	4 - 15	16 - 30	Over 30	Unspecified	Total
Blood pressure normal	Number	34	290	239	46	277	886
	Per Cent	59.6	81.2	65.5	45.5	79.1	72.0
Blood pressure reduced not normal	Number	22	58	110	38	57	285
	Per Cent	38.6	16.2	30.1	37.6	16.3	23.2
Hypertension persists	Number	1	9	16	17	16	59
	Per Cent	1.7	2.5	4.3	16.8	4.5	4.7
TOTALS by age groups		57	357	365	101	350	1,230

As expected, the improvement was less striking in the younger and older patients. The decreased incidence of complete relief in the young age group may well be explained by the fact that many surgeons indicated their preference for interrupted mattress sutures in smaller children with the hope that this technique would favor growth of the anastomosis. However, the constricting effect of this method may be so great, relatively speaking, that significant obstruction may persist postoperatively, in these small vessels.

Persistent hypertension in the older patients can be explained on the basis of organic arteriolar changes resulting from the prolonged hypertension whether it is initiated by the mechanical obstruction alone, the hormonal influences which come into play, or both.

In 1405 survivors the general clinical result was evaluated as being satisfactory in 96.3 per cent and unsatisfactory in 3.6 per cent. The results according to age groups are shown in Table VI.

While specific figures of significance were not obtainable, the consensus seemed clear that the results in the group treated by subclavian-aortic anastomosis were far below average and that this technique should be

TABLE VI
OVERALL CLINICAL RESULT, 1,405 SURVIVORS

Age - Years		0 - 3	4 - 15	16 - 30	Over 30	Unspecified	Total
Satisfactory	Number	108	366	324	77	461	1,354
	Per Cent	99.0	97.3	95.5	92.7	96.2	96.3
Unsatisfactory	Number	1	10	16	6	18	51
	Per Cent	.9	2.6	4.4	7.2	3.7	3.6
TOTALS by age group		109	376	358	83	479	1,405

avoided if possible. The use of the subclavian artery, which is usually grossly dilated, as an autograft has been used and recommended as being preferable to rotating the vessel downward according to the standard technique introduced clinically by Clagett.[9] Although the mortality rate was much higher in the preductal cases than in the postductal, the incidence of unsatisfactory results in the survivors was essentially the same, being 2.7 per cent in the former and 3 per cent in the latter.

CONCLUSIONS

1. This report on the results of the surgical treatment of coarctation of the aorta is based mainly on an up to date evaluation of 1601 cases treated by 36 members of the Surgical Advisory Committee to The Cardiovascular Surgery Section of The American College of Chest Physicians. These results seem to indicate that general application of surgical treatment of coarctation is entirely justifiable.

2. The overall average operative mortality rate was 8.6 per cent, being higher in the younger and older age groups and in the groups where a larger percentage of irreversible complications or uncorrectable associated defects were included.

3. The three most common causes of death were: (a) various cardiac complications including failure with or without associated defects, cardiac arrest or fibrillation, pulmonary edema and shock, together accounting for 37.1 per cent of the deaths; (b) disruption of the anastomosis, causing 22.4 per cent of the postoperative deaths; and (c) hemorrhage at the time of surgery, which caused 12.8 per cent of postoperative deaths.

4. Measures are discussed which should be of value in minimizing serious complications which were unavoidable during the developmental period of this surgical procedure.

5. Over 96 per cent of the survivors obtained a satisfactory overall clinical result.

6. Reasonable limitation of the number of surgeons who are permitted to perform this complicated and unusual type of surgery should be most apt to provide the best results.

CONCLUSIONES

1. Esta información sobre los resultados del tratamiento quirúrgicos de la coartación de la aorta, se basa principalmente en valoración hasta ahora de 1601 casos tratados por 36 miembros del Comité Consejero en Cirugía de la Sección de Cirugía Cardiovascular del American College of Chest Physicians. Entos resultados parecen indicar que la aplicación general del tratamiento quirúrgico de la coartación, es enteramente justificado.

2. La mortalidad global operatoria fué de 8.6 por ciento siendo más alta en los más jóvenes y los mayor edad y en los grupos en que había un porcentaje mayor de complicaciones irreversibles o había asociación con defectos no corregibles.

3. Las tres causas más comunes de la muerte fueron: (a) varias complicaciones cardiacas incluyendo insuficiencia con o sin defectos asociados, paro cardiaco o fibrilación, edema pulmonar y schock, todo esto correspondiendo al 37.1 por ciento de las defunciones; (b) ruptura de la anastomosis causando el 22.4 por ciento de las muertes y (c) hemorragia operatoria que causó el 12.8 por ciento de los decensos operatorios.

4. Se discuten las medidas que pueden emplearse para disminuir las complicaciones graves que fueron inevitables durante el período de desarrollo de la técnica.

5. Más de 96 por ciento de los supervivientes obtuvieron un resultado clínico general satisfactorio.

6. La limitación razonable del número de cirujanos que lleven a cabo esta operación será favorable para obtener los mejores resultados.

RESUME

1. Cette communication sur les résultats du traitement chirurgical de la coarctation aortique est essentiellement basée sur l'étude récente de 1.601 cas traités par 36 membres du Comité Chirurgical Consultatif auprès de la Section Chirurgicale Cardiovasculaire de l'American College of Chest Physicians. Ces résultats semblent indiquer que la généralisation du traitement chirurgical dans la coarctation est parfaitement justifiée.

2. Le taux moyen de mortalité opératoire a été de 8,6%, étant plus élevé chez les groupes de malades très jeunes ou âgés, et chez ceux où l'on notait un plus large pourcentage de complications irréversibles et d'anomalies impossibles à traiter.

3. Les trois causes de mort les plus communes furent: (a) différentes complications cardiaques, y compris la grande insuffisance associée ou non à d'autres anomalies, l'arrêt cardiaque ou la fibrillation, l'oedème pulmonaire, le shock, responsables dans l'ensemble de 37,1% des morts; (b) la rupture de l'anastomose, causant 22,4% des morts post-opératoires, et (c) l'hémorragie au cours de l'intervention, qui est responsable de 12,8% des morts post-opératoires.

4. Les auteurs mettent en discussion lese mesures qui devraient parvenir à diminuer le nombre des complications graves. Il était impossible de les éviter alors que se poursuivait le perfectionnement de cette intervention chirurgicale.

5. Chez plus de 96% des survivants, le résultat clinique fut satisfaisant dans l'ensemble.

6. Une limitation raisonnable du nombre des chirurgiens habilités à pratiquer cette intervention délicate devrait permettre d'obtenir les meilleurs résultats.

SCHLUSSFOLGERUNGEN

1. Dieser Bericht über die Ergebnisse der chirurgischen Behandlung der Aortenstenose geht hauptsächlich aus von einer neuesten Auswertung

von 1 601 Fällen, deren Behandlung durch 36 Mitglieder des beratenden chirurgischen Ausschusses der Sektion für Herz- und Gefäss- Chirurgie des American College of Chest Physicians erfolgt war. Diese Ergebnisse sprechen dafür, das die allgemeine Anwendung der chirurgischen Behandlung der Stenose durchaus gerechtfertigt ist.

2. Die gesamte durchschnittliche Operations-Sterblichkeit betrug 8,6% und war höher für die jüngeren und die älteren Altersgruppen sowie in den Gruppen, in dene ein hoher Prozentsatz von irreversiblen Komplikationen oder begleitender nicht behebbarer Missbildungen vorkam.

3. Die 3 am häufigsten auftretenden Todesursachen waren: (a) verschiedene cardiale Komplikationen einschliesslich Herzversagens mit oder ohne gleichzeitige Missbildungen, Herzstillstand oder Flimmern, Lungenoedem und Schook, die zusammen 37,1% der Todesfälle ausmachten; (b) Ruptur der Anastomose, die 22,4% der postoperativen Todesfälle verursachte; und (c) operative Blutungen, die für 12,8% der postoperativen Todesfälle verantwortlich waren.

4. Es werden Massnahmen erwogen, die von Wert sein können, zur Verringerung ernsthafter Komplikationen, die nur unvermeidbar waren während der Periode der Entwicklung dieser chirurgischen Methode.

5. Mehr als 96% der Überlebenden erlangten ein befriedigends klinisches Gesamtergebnis.

6. Eine angemessene Begrenzung der Zahl von Chirurgen, die diese komplizierte Art von Eingriffen vornehmen, würde am ehesten geeignet sein, die besten Ergebnisse zu ermöglichen.

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Report of the Committee on Chest Diseases in Institutions

Despite heartening evidence of increasing interest on the part of public officials and chest specialists, tuberculosis control in public institutions remains a problem vitally relating to the total tuberculosis control effort.

It cannot be too strongly emphasized that inadequate tuberculosis control measures in such institutions jeopardize the entire community. Contact between individuals in these institutions is generally close and sustained over long periods of time, multiplying opportunities for infection. Ultimately, a majority of the individuals return to the community, thus tending to make the effectiveness of controls in these institutions a valid measure of the community's total tuberculosis control program.

It is essential to develop public recognition and acceptance of this fact, and every method and means of so doing should be utilized. It appears that many of the impediments to effective controls in public institutions have their roots in public apathy, which can only be eliminated by development of informed public interest.

Several organizations are cooperating to achieve better tuberculosis control procedures in institutions.

The American College of Chest Physicians, through its committee, is taking an active part in this cooperative effort. Your committee has been of assistance in many ways; its members visiting institutions and hospitals throughout the United States and several foreign countries, making many contributions to improvement of tuberculosis control programs.

A number of cooperative studies have been completed or are under way. Publications cover the epidemiological and social, as well as medical and surgical aspects of chest diseases, offering significant additions to existing knowledge and assisting in its dissemination.

Improvements in control measures are being achieved despite the many impediments to progress. The value of x-raying all new admissions and of periodic rechecks is generally accepted. Several states perform chest surveys in their institutions every six months. Tuberculin skin testing of new admissions and re-testing of negative reactors is standard procedure in a number of institutions. Pre-employment examinations and periodic rechecks are obligatory in almost all public institutions, with more frequent x-ray film rechecks for personnel assigned to tuberculosis units.

The recently introduced chemotherapy in the treatment of psychiatric conditions is of great interest to chest specialists in mental hospitals and presents a tremendous challenge. The therapeutic approach to the mental and physical diseases in combination has brought about fundamental changes in neuropsychiatric-tuberculosis units. A number of states have intensified their programs and created better facilities for the medical and surgical treatment of tuberculosis, in some instances setting up thoracic surgical centers to meet the needs of several institutions. Occupational therapy and rehabilitation services are available in the majority of large institutions.

There still remain great gaps between existing knowledge and its beneficial application. A general program of prevention should be instituted. All factors which may decrease individual resistance and/or increase the hazards of spreading tuberculosis should be emphasized and combative measures detailed.

Adequate housing and proper food for institutional residents should be made available. All possible effort should be made to develop and maintain proper hygienic habit patterns or alternative controls. Recreational facilities and outdoor activities should be provided.

Periodic chest surveys in all institutions should be a major objective, and all persons with inactive tuberculosis should be rechecked periodically by x-ray film and laboratory tests.

Your committee has reviewed the value of tuberculin skin testing in institutions and believes that new admissions should be given this test, with negative reactors being retested at least once a year. Information accruing

to this procedure would provide important diagnostic help in individual cases and serve as a valuable index to the efficiency of the tuberculosis control program.

Overcrowding in public institutions, a regrettable tradition, may be partially combatted by more efficient utilization of existing facilities and fullest possible application of the latest medical programs. In its overall aspects, however, this remains a problem susceptible to full solution only by construction of new facilities or presently unforseen medical discoveries.

We also discussed the problems of adequate statistical information concerning tuberculosis control in institutions and emphasized the need for more reliable data in this connection. A special effort will be made to obtain the cooperation of agencies interested in this field.

After a reviewal of all pertinent factors, your committee has formulated the following minimum requirements for tuberculosis control programs in penal and mental institutions:

1. The program shall be under the direction of an experienced chest specialist who shall supervise the case finding as well as the clinical work.
2. The program shall incorporate complete case finding procedures including x-raying of all new admissions, pre-employment examinations and periodic institutional surveys, at least annually.
3. Every new admission shall have a tuberculin skin test and negative reactors shall be retested at least annually.
4. Proper clinical and laboratory facilities for diagnosis of chest conditions shall be available.
5. There shall be adequate provisions or arrangements for medical and surgical treatment of tuberculosis.
6. Periodic, frequent follow-up of all inactive cases of tuberculosis in the institution.

Your committee happily notes the trend in mental hospitals toward centralization of care and treatment for active and apparently active tuberculous patients. This should result in improvement in treatment as well as in the institutional tuberculosis control programs. Progress in this area is already reflected in lower institutional tuberculosis incidence and a marked decrease of tuberculosis mortality.

Gains already made, however, only emphasize what can and must be done. Even though tuberculosis control programs in local communities have been intensified, new admissions to neuropsychiatric-tuberculosis units remain relatively high and the tuberculosis problem in public institutions continues to be vital. The vast majority of mental patients afflicted with tuberculosis are cared for in public institutions, i.e., state mental hospitals, veterans' hospitals and psychiatric units of penal institutions. A crusade for improving the conditions in these institutions should be directed at the public and the officials entrusted with institutional administration.

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Editorial: Medical Education Week

MEDICAL EDUCATION WEEK will alert 150 million people to the fact that 82 medical schools are the sole producers of the nation's medical manpower. They train approximately 27,000 undergraduates annually and some 50,000 other medical personnel. They graduate nearly 6,800 doctors annually, but not a sufficient number to keep pace with the increasing demand from communities and hospitals everywhere. From their laboratories flow many of the medical discoveries to conquer disease, prolong life.

Brochures, television, radio and the press will present the facts and figures; help to dispel the myths, as for example, the erroneous notions that only students with "A" averages are admitted to medical schools and that the American Medical Association seeks to control the enrollment and the number of graduates.

But will this propaganda be supported by a concerted effort on the part of the medical schools to create a common bond of interest and understanding between the profession and the laity?

It is amazing in this year of 1957 that the medical school still hides its light under an academic bushel basket. The average layman rarely steps through its doors, and has little opportunity to meet its faculty, scientific investigators and students or hear about the research projects that may have an important bearing on his future health. He remains an entity quite apart from the activities of the school. How is he expected to appreciate fully the magnificent contributions and the needs of medical education that are so widely publicized?

A new type of program to celebrate MEDICAL EDUCATION WEEK seems to be in order; one that will present medicine in a popular vein under the auspices of the medical school; one that will emphasize that the medical school is rendering a vital service to the community.

For several years, The Woman's Medical College has sponsored an annual forum on Founders' Day for its faculty, alumnae, students and the public. The recent meeting held on March 13, 1957 provided both a scientific and popular program, the latter being entitled, "Health in the Headlines." Presentations included "World Nutrition Problems," "Emotions and the Gastrointestinal Tract," "What Makes People Short of Breath," "The Relation of Life Stress to Cardiovascular Symptoms of Disease," and "One May Live Happily with Heart Disease." Among the speakers were: Dr. John B. Youmans, Dean, Vanderbilt University School of Medicine, Nashville; Dr. William D. Stroud, Cardiologist, Pennsylvania Hospital, Philadelphia; Dr. Stewart Wolf, Professor of Medicine, University of Oklahoma School of Medicine, Oklahoma City; Dr. R. Drew Miller, Mayo Clinic, Rochester; Dr. Edwin R. Levine, Assistant Clinical Professor of Medicine, Chicago Medical School; Dr. Maurice S. Segal, Clinical Professor of Medicine, Tufts University School of Medicine, Boston; Dr. George R. Meneely, Director, Research Laboratory, Thayer Veterans Administration Hospital, Nashville; Dr. Arthur M. Master, Cardiologist, Mount Sinai Hospital, New York; and Dr. Henry J. Tumen, Professor, Clinical Gastroenterology, Postgraduate Medical School, University of Pennsylvania, Philadelphia. Discussion and questions from the floor were encouraged and greatly added interest to the meeting. A reception and supper were the highlights of the occasion. It was felt that both the medical school and the community richly gained from the experience.

The plight of the medical school is recognized. It must reach out through the medium of educational health services to the men and women from whom it seeks support. It cannot afford not to.

Burgess L. Gordon, M.D., President
Woman's Medical College of Pennsylvania

The President's Page

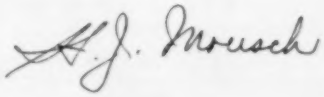
Fads are as prevalent in medicine as they are in other fields of endeavor. They may be, and usually are, of fleeting duration, uncertain heritage and dubious value, destined for an early demise. Fortunately, true innovations enjoy a kinder fate, and contribute greatly to the advancement of medicine and the care of the sick.

It is often difficult to explain or to understand what ingredients are necessary to stimulate the development of a fad in medicine. Perhaps it is the accidental coaptation of scientific minds and information at the proper time and place. More often, however, it is the illness of a great leader and personality, or the occurrence of a great epidemic or national catastrophe, such as war, that concentrates the attention of the medical profession upon a particular disease. Again, it may be the skillful organization of a group of physicians and research workers who have mastered the technic of arousing the interest of the medical profession and the public in a certain problem.

With the proper conception and organization, a fad that might otherwise be most ephemeral can be made to contribute greatly to the advancement of medicine, for it may be used to incite the concentration of many minds upon a given problem, with the prospect of more prompt resolution than would be possible if each investigator were to work alone. I need only call your attention to what such mass effort has accomplished in the field of atomic energy, in the apparent prevention of poliomyelitis, in the control of tuberculosis and in the virtual eradication of syphilis.

Yet, in our enthusiasm for new fads, no matter how commendable, it is important that we do not, thereby, neglect unfinished problems and investigations that pertain to our own field. In fact, care must be exercised that neglect is not mistaken for accomplishment. For instance, we all are stirred by the impressive advancements that have been made in the field of intracardiac surgery, but it is nevertheless important that we do not forget the other thoracic problems which remain, such as pulmonary emphysema, tuberculosis and cancer of the lung. In view of the nature of the recent untimely death of Dr. Evarts A. Graham, it would seem especially appropriate for us now to renew our efforts in the conquest of that dread disease, cancer of the lung, against which he so valiantly fought but which ultimately conquered him.

Certainly, it is farthest from my intention to deprecate in any way the marvelous work that is being done against cardiovascular disease, which constitutes one of the major problems of medicine today. Rather, I simply wish to point out that many another problem remains in the field of thoracic disease, challenging our attention. Such problems must not be overlooked. Thus it is that, in the face of the many demands that are being made upon each and every physician's time and pocketbook for the support of many worthy causes in medicine, it is possible that we can learn much from those who have been successful in dealing with fads of the past.



23RD ANNUAL MEETING OF THE COLLEGE

New York City will be host to the 23rd Annual Meeting of the College, being held at the Hotel Commodore, May 29 through June 2, 1957. The American Medical Association will hold its 106th Annual Meeting in New York City, June 3-7.

A special section in the March issue of *Diseases of the Chest* was devoted to the scientific program for the 23rd Annual Meeting. This is one of the finest programs ever to be presented at a College meeting and you will not want to miss it.

All physicians who plan to attend the annual meeting are urged to submit Advance Registration Forms, which may be found in the March issue of the College journal. Advance Registration Forms from *non-members* must be accompanied by the registration fee of $25.00. Additional copies of the program may be obtained by writing to the Executive Offices of the College, 112 East Chestnut Street, Chicago 11, Illinois.

Please write directly to the Hotel Commodore, New York City, for reservations; a coupon for this purpose may be found on page xviii of this issue of the journal.

Ladies Activities

The Ladies Reception Committee for the 23rd Annual Meeting of the College has prepared a delightful program of events for the visiting ladies. Mrs. Alfred S. Dooneief, Chairman, and Mrs. Alvan L. Barach, Co-Chairman, have announced the following functions:

Thursday, May 30

12:30 p.m.—Luncheon, Waldorf Astoria Hotel
Featuring an exhibition by the Arthur Murray Dancers, who will also give lessons in the "CHA-CHA." There will be a hostess at each table to assist the ladies in locating old friends and making new ones.

Friday May 31

8:30 p.m.—Theatre Party—"My Fair Lady"
Only 100 tickets are available for this performance and ladies from outside the Greater New York area will be given preference. Reservations must be made in advance and will be accepted in the order received. The Ladies Reception Committee will be pleased to be of assistance in obtaining tickets for other good shows. All theatre tickets will be held at the Ladies Registration Desk and must be claimed by 10:30 a.m. Friday, May 31.

Saturday, June 1

9:00 a.m.—Breakfast, B. Altman & Company
A fashion show will be presented, door prizes given, and a corsage for every lady.

6:00 p.m.—College Convocation, Hotel Commodore

7:00 p.m.—Cocktail Party
Sponsored by The Panray Corp., New York City

7:30 p.m.—Annual Presidents' Banquet

9:00 p.m.—After-Dinner Dance
Sponsored by the New York State Chapter of the College
Music by Sonny Kippe and his Orchestra

Sunday, June 2

The Ladies Reception Committee is preparing a calendar of worthwhile events in New York City, including shows, movies, art exhibits, the United Nations, concerts, etc. The Committee will be pleased to assist in arrangements for tickets and transportation.

All ladies attending the meeting are invited to register and receive guest badges. Tickets ordered for all functions will be held at the Ladies Registration Desk for pick-up.

Ladies Reception Committee

MRS. HERMAN J. MOERSCH.....*Honorary Chairman*
MRS. ALFRED S. DOONEIEF.....*Chairman*
MRS. ALVAN L. BARACH.....*Co-Chairman*

Breakfast Arrangements.....MRS. ARTHUR AUFSES
Theatre Tickets.....MRS. JAMES S. EDLIN
Luncheon Arrangements.....MRS. HENRY J. HEIMLICH
Registration.....MRS. EMIL NACLERIO
Events Calendar.....MRS. JOEL SCHWARTZMAN

MRS. PETER AMAZON
MRS. ALVIN BAKST
MRS. HYLAN A. BICKERMAN
MRS. ALLAN BLOOMBERG
MRS. ISADORE BOBROWITZ
MRS. ARTHUR CRACOVANER
MRS. SIMON DACK
MRS. ISRAEL EPSTEIN
MRS. LEONARD EVANDER
MRS. HARRY GOLEMBE
MRS. EDWIN GRACE
MRS. CHARLES HAMILTON
MRS. GEORGE F. HERBEN
MRS. LEW HOCHBERG
MRS. IRVING KANE
MRS. IRVING KROOP
MRS. ADRIAN LAMBERT
MRS. HAROLD LYONS
MRS. DONALD R. MCKAY
MRS. EDGAR MAYER
MRS. GEORGE ORNSTEIN
MRS. COLEMAN B. RABIN
MRS. NATHANIEL REICH
MRS. ALFRED RING
MRS. ARNOLD RODMAN
MRS. ELI RUBIN
MRS. MORRIS RUBIN
MRS. ISRAEL STEINBERG
MRS. SAMUEL A. THOMPSON

PAN-AMERICAN WEEK AND WORLD HEALTH DAY

The week of April 8-14, 1957 has been set aside as Pan American Week and April 7, 1957 as World Health Day, which also marks the Ninth Anniversary of the World Health Organization. On this occasion, the American College of Chest Physicians wishes to salute all the societies engaged in furthering the health of peoples throughout the world.

The American College of Chest Physicians, since 1940, when the first College Chapter outside of the United States of America was organized in Cuba, has been developing a world society of physicians and surgeons who specialize in chest diseases. There are presently 66 chapters and 5,709 members in 88 countries and territories.

The College journal, *Diseases of The Chest*, enjoys a world circulation of 7,850 and for the convenience of its international readership, the summaries of the scientific articles are translated into French, Spanish and German. Since 1950, the Council on International Affairs of the College has sponsored four international congresses:

1950 Rome, Italy
1952 Rio de Janeiro, Brazil
1954 Barcelona, Spain
1956 Cologne, Germany

The Fifth International Congress on Diseases of the Chest will be held in Tokyo, Japan, September 7-11, 1958. These international congresses provide a common forum for the chest specialists from many countries to present papers on the most recent advances in the diagnosis and treatment in heart and lung diseases. Throughout the years, the College has recognized the achievements of several internationally known chest specialists with the presentation of the coveted Gold Medal of the College. Among those who have been awarded the College medal are:

Professor Manoel de Abreu, Brazil
Sir Alexander Fleming, England
Professor Jorgen Lehmann, Sweden
Professor Raul F. Vaccarezza, Argentina
Professor Attilio Omodei Zorini, Italy

Medicine, like art and music, is international in scope. Physicians, who are the healers and comforters of the sick, have much to contribute to better understanding and goodwill. By the joining of hands, the physicians of the world can be a great influence in shaping our destiny.

Andrew L. Banyai, M.D., Chairman
Council on International Affairs

PAN-AMERICAN MEETINGS

The National Congress on Tuberculosis and Silicosis of Mexico will be held in Monterrey, Mexico, April 21-27, 1957. Dr. Andrew L. Banyai, Milwaukee, Wisconsin, Chairman of the Council on International Affairs of the College, will present a paper on "The Technique and Clinical Aspects of Artificial Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis" and will also appear on a panel discussion on "Conservative Relaxation Therapy in Pulmonary Tuberculosis." Dr. Banyai will speak before the annual meeting of the Mexican Chapter which will be held in Monterrey. Dr. Donato G. Alarcón, Regent of the College for Mexico, will present a paper at the chapter meeting on lung cancer.

Other physicians from the United States will participate in the Congress and present the following papers:

Charles P. Bailey, Philadelphia, Pennsylvania, "Cardiac Surgery with the Use of the Heart-Lung Bypass."

J. Maxwell Chamberlain, New York, New York, "The Results of Segmental Resection Followed from Five to Ten Years."

Edward H. Robitzek, Staten Island, New York, "Treatment of Human Tuberculosis with Cycloserine."

Arpad Berczeller, Staten Island, New York, "Protection of Dihydrostreptomycin Against Thermal Decomposition by Admixture of Isoniazid."

Watts R. Webb, Jackson, Mississippi, "Progress in Experimental Cardiac Transplantation."

Following the meetings in Monterrey, Dr. Banyai will go to Medellín, Colombia as the official representative of the American College of Chest Physicians at the ULAST Congress, to be held April 27-May 1. In his capacity as Chairman of the Council on International Affairs of the College, he will speak at the breakfast meeting of the Council on Pan-American Affairs on May 1. Dr. Jose Ignacio Baldo, Caracas, Venezuela, Chairman of the Council on Pan-American Affairs of the College and Regent for Venezuela, will preside at the meeting. Dr. Rafael Mejia C., Medellin, Governor of the College for Colombia, is President of the Congress, and Dr. Carlos Arboleda Diaz, Bogota, Regent of the College for Colombia, serves as Vice President. Dr. Fernando D. Gomez, Montevideo, Regent of the College for Uruguay, is Secretary-General of ULAST.

College Chapter News

ALABAMA CHAPTER

The annual meeting of the Alabama Chapter will be held at the Admiral Semmes Hotel, Mobile, on April 17. The chapter will present the following program:

2:00 p.m. "Alveolar Cell Carcinoma of the Lung"
Charles R. Kessler, Birmingham

"Experiences with Prefabricated Nylon Arterial Grafts"
Sterling Edwards, Birmingham

"Medical Aspects of Cardiovascular Surgery"
Joseph F. Uricchio, Philadelphia, Pennsylvania

"Anti-tuberculosis Drugs and Their Present Mode of Usage"
Robert K. Oliver, Montgomery

5:00 p.m. Business meeting and election of officers

5:30 p.m. Social Hour

ARKANSAS CHAPTER

The Arkansas Chapter of the College will hold its annual meeting at the Marion Hotel, Little Rock, April 22. An x-ray conference will be presented, followed by a dinner and business meeting.

CALIFORNIA CHAPTER

The annual meeting of the California Chapter will be held at the Ambassador Hotel, Los Angeles, April 27. The following program, arranged by Dr. Elmer C. Rigby and his committee, will be presented.

Morning Session

Marvin S. Harris, Los Angeles, Chapter President, presiding

9:15 a.m. "'Pembine' Type Conference"
Moderator—David Salkin, San Fernando
Ten consecutive cases discharged after July 1, 1955 from the Long Beach Veterans Administration Hospital will be presented by Dr. LeRoy Hyde

"Interesting Cases I Have Seen—What Would be Your Modus Operandi?"
Moderator—Samuel J. Sills, Los Angeles
J. W. Birsner, Bakersfield; J. F. Boyle, Los Angeles; E. P. Brauner, Visalia; I. A. Breckler, Sherman Oaks; J. N. Briggs, Van Nuys; B. H. Cotton, Los Angeles; Stephen Elek, Los Angeles; Seymour M. Farber, San Francisco; James Kieran, Oakland; H. D. Peabody, San Diego; Sidney J. Shipman, San Francisco; Harold G. Trimble, Oakland; Travis Winsor, Los Angeles; W. G. Winter, Fresno; and Thomas B. Wiper, San Francisco

12:00 noon Luncheon and business meeting
Presentation of Chapter's Annual Award to Frank S. Dolley, Los Angeles and Leo Eloesser, San Francisco by Lyman A. Brewer, III, Los Angeles and Thomas B. Wiper, San Francisco

Afternoon Session

2:00 p.m. "Evaluation of Dyspnea in Pulmonary Emphysema by Application of Therapeutic Procedures"
Alvan L. Barach, New York, New York

"Newer Aspects of Surgery for Acquired and Congenital Heart Disease"
Frank L. Gerbode, San Francisco

"The Present Status of Angiocardiography"
Charles T. Dotter, Portland, Oregon

Diagnosis and Therapy—New and Review

"Tangential Chest Injuries"
Marion L. Connerley, San Diego

"Pyridoxine Deficiency and Pulmonary Tuberculosis"
William Mandel, San Francisco

"Present Status of Lucite Spheres in Collapse Therapy"
William Gyarfas and Alfred Goldman, Duarte

"Coronary Angiography"
Bernard J. O'Loughlin, Los Angeles

5:30 p.m. Social Hour

FLORIDA CHAPTER

The ninth annual meeting of the Florida Chapter will be held in Hollywood, May 5. Dr. George L. Baum, Coral Gables, and his committee have arranged the following program:

9:00 a.m. "Preoperative Evaluation of the Geriatric Bronchogenic Carcinoma Patient"
Charles F. Tate, New York City
Discussor: Asher Marks, Miami

"Serum Glutamic Oxaloacetic Transaminase, Serum Glutamic Pyruvic Transaminase and Serum Lactic Dehydrogenase in Myocardial Infarction"
John S. LaDue, New York City
Discussor: J. Frederick Woessner, Miami

"Middle Lobe Syndrome"
Harold C. Spear, Miami
Discussor: DeWitt C. Daughtry, Miami

"Use of Extracorporeal Circulation in Open Heart Surgery"
Robert Litwak, Miami
Discussor: Philip Samet, Miami Beach

"Alterations of the Electrocardiogram in Neuro-psychiatric Patients"
A. A. Leonidoff, Poughkeepsie, New York
Discussor: Louis Lemberg, Miami

12:15 p.m. Luncheon and business meeting

2:00 p.m. Panel discussion—"Management of Pulmonary Tuberculosis"
Moderator: Jack Reiss, Coral Gables
Panel: Ivan Schmidt, West Palm Beach; Hawley H. Seiler, Tampa, and S. D. Doff, Jacksonville

Panel discussion—"Chronic Pulmonary Emphysema"
Moderator: M. Eugene Flipse, Miami
Panel: Philip Samet, Miami Beach; Asher Marks, Miami; Jerome Benson, Miami Beach

X-ray Conference
Moderator: M. Jay Flipse, Miami

(Those in attendance are requested to bring x-ray films for discussion after presenting a brief and pertinent clinical history.)

GEORGIA CHAPTER

The Georgia Chapter will have a luncheon meeting in Savannah, May 5. Dr. Donald Effler of Cleveland, Ohio, will be guest lecturer.

MINNESOTA CHAPTER

The annual meeting of the Minnesota Chapter will be held at the Hotel Lowry, St. Paul, May 12. The following program will be presented:

1:00 p.m. Registration

2:00 p.m. "Storage Phenomena of the Myocardium"
William F. Mazzitello, St. Paul

"Use of Induced Cardiac Arrest in Open Heart Surgery
Peter Allen and C. Walton Lillehei, Minneapolis

"Evaluation of Aerosol Bronchodilators in Bronchitis and Emphysema"
R. Drew Miller, Rochester

"Resectional Surgery for Tuberculosis in Elderly People"
Thomas J. Kinsella, Minneapolis

"Molar Sodium Lactate in Acute Adrenalin-Fast Asthmatics"
J. S. Blumenthal, E. B. Brown, and G. S. Campbell, Minneapolis

3:40 p.m. Intermission and business meeting

4:00 p.m. Diagnostic Clinico-Pathologic Conference
Moderator: Jesse E. Edwards, Rochester
Panel: Leo Rigler, Minneapolis; John F. Briggs, St. Paul; Arthur M. Olsen, Rochester; Thomas Parkin, Rochester; and Ralph Smith, Minneapolis

5:30 p.m. Social Hour

6:30 p.m. Dinner
"Adventure and Re-Adventure in Cuba"
Philip S. Hench, M.D., Rochester, Minnesota

NEW ENGLAND STATES CHAPTER

Dr. Henry R. Viets, Brookline, Massachusetts, will address the meeting of the New England States Chapter on April 17 at the New England Deaconess Hospital in Boston. Dr. Viets title is "Thymectomy for Myasthenia Gravis." A special meeting of the chapter was held on March 27, at which Dr. Takashi Nakamura of Sendai, Japan, spoke on "Bronchial Artery to Pulmonary Artery Shunts in Pulmonary Fibrosis."

OHIO CHAPTER

The annual meeting of the Ohio Chapter will be held at the Veterans Memorial Building, Columbus, May 15. The following program will be presented:

2:00 p.m. "Pulmonary Fungus Diseases"
Robert J. Atwell, Columbus
"Pulmonary Function Studies"
George W. Wright, Cleveland
"Intracardiac Surgery under Direct Vision"
James A. Helmsworth, Cincinnati

3:45 p.m. Business Meeting

OKLAHOMA CHAPTER

The Oklahoma Chapter will present a Consecutive Case Conference at the Veterans Administration Hospital, Oklahoma City, April 14. Guest speakers will be Dr. I. D. Baronofsky, New York City, and Dr. H. William Harris, Salt Lake City, Utah.

PENNSYLVANIA CHAPTER

The annual meeting of the Pennsylvania Chapter will be presented in Harrisburg on April 25. Following is the program which will be presented:

10:30 a.m. "Report on the 1957 Veterans Administration-Army-Navy Conference on Chemotherapy"
Archibald Cohen, Butler, Pennsylvania
"The Practical Management of the Patient with Emphysema"
Richard T. Cathcart, Philadelphia
"The Current Status of Bronchiectasis"
J. Antrim Crellin, Philadelphia and John M. Snyder, Bethlehem

1:00 p.m. Luncheon

2:00 p.m. "Indications for Angiocardiography and Cardiac Catheterization"
Thomas J. E. O'Neill and Gerardo Voci, Philadelphia
"Fads and Fashions in the Treatment of Pulmonary Tuberculosis"
Ross K. Childerhose, Harrisburg

A question period will follow each presentation.

TEXAS CHAPTER

The annual meeting of the Texas Chapter will be held at the Adolphus Hotel in Dallas, Sunday, April 28. Following is the program:

Morning Session

Chairman: Walter C. Brown, Corpus Christi, Chapter President

9:00 a.m. "Preliminary Report on Treatment of Diabetes Mellitus with Orinase in Pulmonary Tuberculosis"
E. H. Roberts and Paul E. Johnson, San Antonio
"Office Bronchography"
John A. Wiggins, Fort Worth
"New Approach to Funnel Chest Repair with External Braces"
Robert Wilkens, Corpus Christi
"Diagnosis and Management of Surgical Diseases of the Chest in Children"
Thomas H. Burford, St. Louis, Missouri
Panel discussion: "The Management of Inoperable Lung Cancer"
Moderator: Robert B. Morrison, Austin
Panel: Howard T. Barkley, Houston; Clifford Howe, Houston; John Mallams, Dallas; David McCullough, San Antonio; Martin Schneider, Galveston; and Robert R. Shaw, Dallas

12:30 p.m. Luncheon and business meeting
Remarks by Herman J. Moersch, President, American College of Chest Physicians, Rochester, Minnesota

Afternoon Session

Chairman: W. D. Anderson, San Angelo

2:00 p.m. "The Value of Endoscopy in the Diagnosis of Bronchoesophageal Disease" (Charles M. Hendricks Memorial Lecture)
Herman J. Moersch, Rochester, Minnesota

"Single Stage Thoracoplasty Using a Simple Technique to Control Paradoxical Chest Wall Motion"
Buford H. Burch, Patton, California, and Lawrence M. Shefts, San Antonio

"Observations on the Use of an Improved Flexible-Tipped Bronchoscopic Aspirating Tube"
Robert B. Morrison, Austin

"Professor Miller's X-Ray Quiz"
Jarrell E. Miller, Dallas

WISCONSIN CHAPTER

The Wisconsin Chapter will hold its annual meeting at the Schroeder Hotel, Milwaukee, May 5. Following is the program to be presented:

2:00 p.m. "Medical Treatment of Bronchiectasis"
F. Edmund Donoghue, Rochester, Minnesota

"Importance of Transthoracic Lung Biopsy in Establishing an Accurate Diagnosis"
Karl P. Klassen, Columbus, Ohio

"Experiences with the Clinical Application of Extracorporeal Circulation"
F. Henry Ellis, Rochester, Minnesota

"Tumors of the Lung"
J. Maxwell Chamberlain, New York City

"Cyanotic Diseases in Children"
Benjamin M. Gasul, Chicago, Illinois

"The Destroyed Pulmonary Segment"
Richard H. Overholt, Boston, Massachusetts

NEW JERSEY CHAPTER

Dr. Burgess L. Gordon, Philadelphia, Pennsylvania, President-Elect of the College, presented the Third Selman Waksman Lecture sponsored by the New Jersey Chapter at their meeting in Newark, March 27.

CUBAN CHAPTER

New officers of the Cuban Chapter, elected at their meeting in February, are:

President:	Armando Nuñez Nuñez, Havana
Vice-President:	Luis P. Romaguera, Havana
Secretary-Treasurer:	Rodrigo A. Bustamente, Havana

PUERTO RICO CHAPTER

At the fourth annual meeting of the Puerto Rico Chapter, the following officers were elected:

President:	H. Martinez Villafane, Santurce
Vice-President:	J. R. Marchand, Santurce
Secretary-Treasurer:	J. L. Porrata, Hato Rey

PHILIPPINE CHAPTER

The following officers for 1957 have been elected by the Philippine Chapter:

President	Godofredo R. Hebron, Manila
President-Elect	Jose Celis, Quezon City
Vice-President	Montano Perez Conde, Manila
Secretary-Treasurer	Priscilla J. Tablan, Quezon City (re-elected)

QUEBEC CHAPTER

At the annual meeting of the Quebec Chapter, the following officers were elected for 1957:

President	Gaetan Jarry, Montreal
Ist Vice-President	Jonathan F. Meakins, Montreal
2nd Vice-President	Alphonse L'Esperance, Ste. Foy
Secretary-Treasurer	Andre Mackay, Montreal

VENEZUELA CHAPTER

The Venezuela Chapter of the College held its annual meeting in Merida at which time the following officers were elected:

President	Cesar Rodriguez, Caracas
Vice-President	Louis Gomez Lopez, Barquisimeto
Secretary-Treasurer	Rogelio Valladares, Caracas

BARCELONA (SPAIN) CHAPTER

The following officers were elected by members of the Barcelona Chapter at their annual meeting.

President:	Conrad Xalabarder Puig, Barcelona
Vice President:	Luis Trias Giro, Barcelona
Secretary:	Modesto Gonzalez Ribas, Barcelona
Treasurer:	Francisco Coll Colome, Barcelona (re-elected)

HONG KONG AND CHINA CHAPTER

A meeting of the Hong Kong and China Chapter was held at the Hong Kong Sanatorium and Hospital with Dr. Kenneth Hui presiding. New chapter officers are:

President:	Mary Aquinas, Hong Kong
Vice President:	Li Shu Pui, Hong Kong
Secretary-Treasurers:	Stephen D. Sturton, Hong Kong
	M. W. Look, Hong Kong

Dr. Aquinas was elected to represent the Hong Kong and China Chapter of the College at the 14th International Tuberculosis Conference at New Delhi, India.

Dr. Li Shu-Fan, Regent of the College for China, gave a talk on the International Congress of the College, held in Cologne, Germany, in August, 1956. Dr. Li presented a color-film with his talk.

College News Notes

Dr. Herman J. Moersch, Rochester, Minnesota, President of the American College of Chest Physicians, was recently elected President of the Mayo Clinic Staff.

Dr. Daniel L. Finucane, formerly Superintendent and Medical Director of the Glenn Dale Hospital, Glenn Dale, Maryland, has been appointed Commissioner of Health of the District of Columbia by the Commissioners of the District.

Drs. C. Walton Lillehei and **Richard A. DeWall** of the University of Minnesota Medical School, Minneapolis, received the American Association for the Advancement of Science—Ida B. Gould Award for research in cardiovascular problems. They were honored for their work in open heart surgery in which they utilized a simple pump oxygenator, since adopted throughout the world.

Dr. Julius B. Novak, Chicago, Illinois, has been appointed by Governor William G. Stratton to serve on the Advisory Committee on Tuberculosis Control in the Illinois Department of Public Welfare.

The following new officers of the Memphis Thoracic Society for 1957 are Fellows of the College: **Drs. F. H. Alley,** President; **E. F. Skinner,** Vice President; and **Michael M. Marolla,** Secretary-Treasurer.

Prof. Dr. Carlos Bento, Governor of the College for Rio Grande do Sul, Brazil, has been elected President of the Tuberculosis Society of Rio Grande do Sul.

Dr. Benjamin M. Gasul, Chicago, Illinois, has won the award for Scientific Exhibit at the National Medical Meeting in Chicago. Dr. Gasul's prize-winning exhibit showed x-ray studies of congenital malformations of the heart. **Dr. E. H. Fell** of Chicago was one of the collaborators in the exhibit.

The Arizona Chapter of the College sponsored a Symposium on Coccidioidomycosis on February 11-13 in Phoenix, in conjunction with the Arizona State Department of Health, the Communicable Disease Center of Phoenix, the United States Public Health Service of Atlanta, Georgia, and in cooperation with the Phoenix City Health Department. Members of the College who participated in the symposium were **Drs. Robert J. Anderson,** Atlanta, Georgia; **Bert H. Cotton,** Los Angeles, California; **William A. Winn,** Springville, California; **O. J. Farness,** Tucson, Arizona; **D. W. Melick,** Phoenix, Arizona.

Dr. S. J. Shane, Halifax, Nova Scotia, has been appointed assistant professor of medicine at Dalhousie University, Halifax. Dr. Shane will also assume directorship of the Halifax Tuberculosis Hospital and will be affiliated with the new cardio-respiratory unit being established by Dalhousie University and Victoria General Hospital. Dr. Shane was formerly Superintendent of the Point Edward Hospital in Sydney, Nova Scotia.

ANNOUNCEMENT

The 37th Annual Meeting of the American Association for Thoracic Surgery will be held at the Palmer House, Chicago, May 4, 6, 7, 1957. Dr. William E. Adams, Chicago, is in charge of arrangements for the meeting. Dr. Hiram T. Langston, Chicago, is secretary of the association.

BOOK REVIEW

BIOCHEMICAL MECHANISMS IN INFLAMMATION by Valy Menkin, Charles C Thomas, Springfield, Illinois, second edition 1956, 438 pages, $9.50.

Despite the broad title of this book, it is primarily concerned with the author's research into various substances which he has extracted from exudates. These substances have physiological effects on the host. The author is well known for his work on leukotaxine which, when injected into the body, produces increased capillary permiability and mobilization of leukocytes. In addition to this, however, the author has also isolated the following substances: exudin, thermolabile and thermostabile leukocytosis promoting factors, necrosin, pyrexin and two leukopenic factors. These are all presumed to be liberated by damaged cells under slightly differing conditions.

The author has done a tremendous amount of work on these substances, and a good deal of what he has done has been confirmed by other workers. This is a rather narrow field, however and can best be discussed by those who have had personal experience in research along these particular lines. The author does attempt to branch out from the discussion of these substances to a discussion of infflammation in general, allergic reactions, hormonal effects on inflammation and carcinogenesis. All aspects of inflammation and the other problems just outlined are discussed in relation to the substances which the author has extracted.

This book has numerous good points, among them, a tremendous amount of information that has been gathered by the author's many years of work in this field, excellent references to other work in the field and some good illustrations of various aspects of inflammation. This book suffers from the fact that any attempt at systematizing such an enormous field in a limited space leads to unavoidable simplification and to some statements to which other workers might take exception.

It is unfortunate that the author has done himself a disservice by adopting an injudicious and at times even an argumentative attitude toward other workers and other work in this field.

Ann Pollak, M.D.

MEDICAL SERVICE BUREAU

POSITIONS WANTED

General and thoracic surgeon, 35, F.C.C.P., desires association with clinic or established surgeon, west coast preferred. Completing 5-year residency program in July. Six years prior experience in private practice, sanatorium work, and endoscopy. Qualified for board certification in general and thoracic surgery. Please address inquiries to Box 288B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Chest physician, married, 20 years hospital experience, seeks position as medical director. Available in May. References. Please address inquiries to Box 289B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Physician—board qualified in chest diseases, main experience in pulmonary function studies and chronic lung diseases, especially non-tuberculous, to be released from active duty, US Navy in September, 1957, desires position with university affiliation and research facilities. Please address inquiries to Box 290B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

POSITIONS AVAILABLE

Physicians wanted: immediate opening for two part-time physicians qualified to interpret survey x-rays and standard chest films. Physicians desiring semi-retirement in Florida will be considered. Salary open. Write Wilson T. Sowder, M.D., State Health Officer, Florida State Board of Health, PO Box 210, Jacksonville 1, Florida.

Assistant Medical Director wanted for 114-bed tuberculosis hospital. Salary $8500-$9500, complete maintenance. Apply Medical Director and Superintendent, District Four Tuberculosis Hospital, Ashland, Kentucky, or State Tuberculosis Hospital Commission, New State Office Building, Frankfort, Kentucky.

Qualified physician wanted for Medical Staff with training or experience in general medicine or tuberculosis. Must have or be able to secure Texas license. Night duty kept to a minimum. Pleasant working conditions in progressive system. New, completely modern, air-conditioned hospital nearing completion. City of over 50,000 population located in the heart of scenic East Texas. Excellent school system, churches, civic and social organizations. Many fine lakes and heavily wooded areas offer excellent outdoor sports. Salary range from $9,900 to $10,000 expected to be increased on new budget. Tuberculosis experience preferred, but not required. Apply immediately to: Personnel Officer, East Texas Tuberculosis Hospital, Box 2003, Tyler, Texas.

CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

23rd Annual Meeting, American College of Chest Physicians
Hotel Commodore, New York City, May 29-June 2, 1957

Fifth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Tokyo, Japan, September 7-11, 1958

CHAPTER MEETINGS

Tennessee Chapter, Nashville, April 10
Arizona Chapter, Yuma, April 12
Oklahoma Chapter, Okla. City, April 14
Alabama Chapter, Mobile, April 17
Arkansas Chapter, Little Rock, April 22
Penn. Chapter, Harrisburg, April 25
Calif. Chapter, Los Angeles, April 27
Texas Chapter, Dallas, April 28
Georgia Chapter, Savannah, April 30
N. J. Chapter, Atlantic City, May 1
Florida Chapter, Hollywood, May 5
Wisconsin Chapter, Milwaukee, May 5
Minnesota Chapter, St. Paul, May 12
Ohio Chapter, Columbus, May 15
Illinois Chapter, Chicago, May 23

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J. Lloyd Eaton, M.D., Oakland
Gerald L. Crenshaw, M.D., Oakland
Glenroy N. Pierce, M.D., San Francisco
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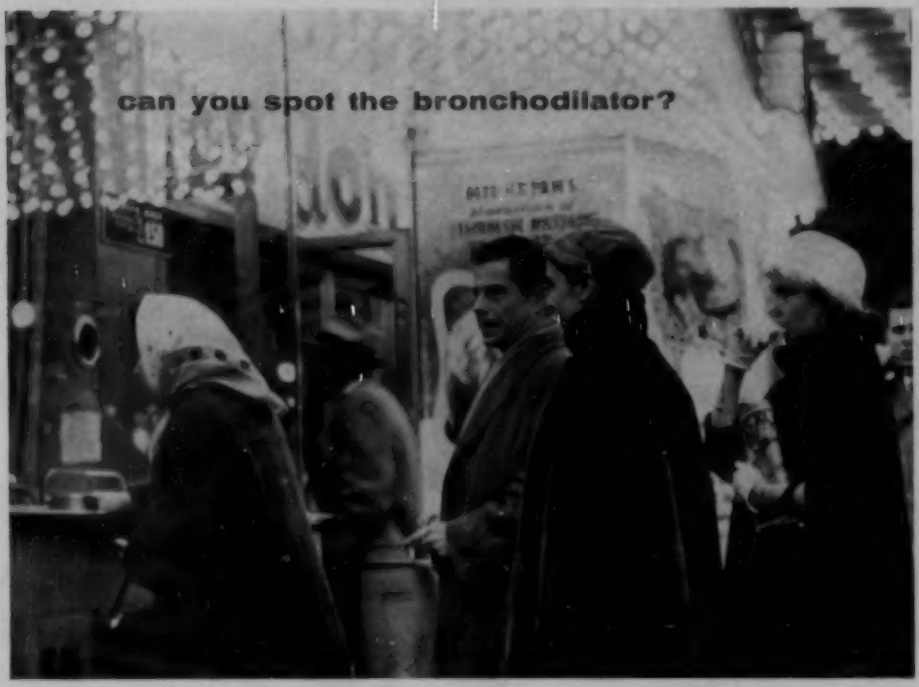

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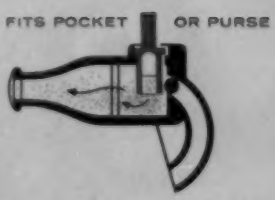

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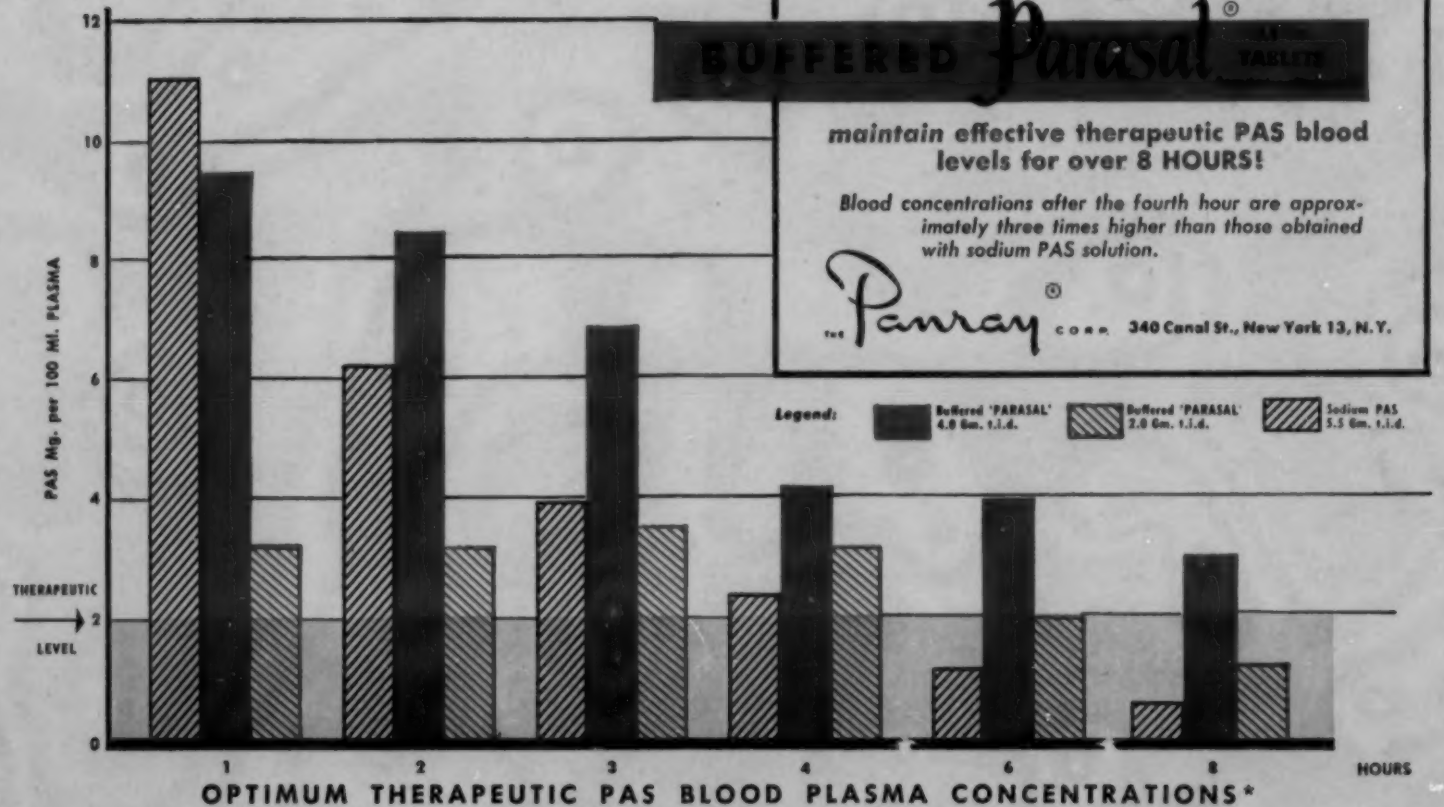

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Ref.: Deeb, E. N. & Vitagliano, G.R.: A. Rev. Tuber. & Pul. Dis.: 72,543-7 (Oct. '55

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